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Sponsor:

Dynamac Corporation 11140 Rockville Pike Rockville, Maryland 20852

FINAL REPORT

Study Title:

Subchronic Toxicity Study in Rats with m-Xylene

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Hazleton Laboratories America, Inc. 1330-B Piccard Drive Rockville, Maryland 20850-4373

Laboratory Project Identification:

HLA Study No. 2399-108

May 27, 1988

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PROTOCOL AMENDMENT

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STUDY DIRECTOR: Say W. Wolfe
DATE: 8/5/86



-2-

COMPLIANCE STATEMENT Subchronic Toxicity Study in Rats with m-Xylene

This study was conducted in compliance with the Good Laboratory Practice Regulations as set forth in Title 40 of the U.S. Code of Federal Regulations Part 160. There are no significant deviations from the aforementioned regulations which affected the quality or integrity of the study or the interpretation of the results in the report.

Study Director:

Gary W. Wolfe, Ph.D. D.A.B.T.

Date

Life Sciences Division

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- 3 -

QUALITY ASSURANCE UNIT

Project Title: Subchronic Toxicity Study in Rats with m-Xylene

Project No.: 2399-108

Quality Assurance Review of the final report was conducted according to the procedures described in the standard operating procedures of the Report Review Section of the Quality Assurance Unit, and according to the general requirements of the Good Laboratory Practice Regulations issued by the Environmental Protection Agency for compliance on or after May 2, 1984. The final report review was conducted and the findings were reported to management and to the study director on the following dates:

Final Report Review	Findings Reported	Reviewer
Protocol 4/10/86	4/10/86	D. Goldsteen
Inspection 1 4/22, 24/86	5/9/86	D. Goldsteen
Inspection 2 9/2, 7, 8/86	7/15/86	D. Goldsteen
Final Report 8/28, 29; 9/2-5/86	9/9/86	K. Glenn
12/2/86	12/8/86	K. Reilly
5/26, 27/88	5/27/88	E. Jenkins

Final Report Reviewer Quality Assurance Unit Date Released

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STUDY IDENTIFICATION Subchronic Toxicity Study in Rats with m-Xylene

HLA Study Number

2399-108

Test Material

m-Xylene (CAS 108-38-3)

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Study Timetable Initiation Date Termination Date

April 11, 1986 July 16, 1986

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SUMMARY

The test material, m-Xylene (CAS 108-38-3), was administered to male and female rats by oral gavage in order to evaluate its subchronic toxicity. Dose levels were 0, 100, 200, and 800 mg/kg/day (Groups 1 through 4, respectively), with 20 animals/sex/group dosed daily for at least 90 days. Criteria evaluated included mortality, clinical signs, body weights, food consumption, ophthalmologic examinations, hematology, clinical chemistry, organ weights, organ-to-body weight ratios, gross pathology, and histopathology.

Mortality was significantly increased in male Group 3 and female Groups 3 and 4; however, based on histopathology findings, these deaths were most likely the result of vehicle and/or compound aspiration. Salivation was frequently observed in both sexes of Group 4 and only rarely in the other treated groups. Total body weight gain was significantly decreased in male Groups 3 and 4, and female Group 4. Food consumption was significantly decreased from Week 1 to 5 in Group 4 males and from Week 6 to 9 in Groups 3 and 4 males. A few clinical pathology parameters were significantly increased or decreased and with one exception (female Group 3), all were in Group 4. A few significant changes were seen in absolute or relative organ weights, all of which were in male Group 4. The most commonly observed lesions at necropsy were in the lungs (mottled and failure to collapse). These lesions were only seen in the animals found dead. No apparent compound-related effects were present in the ophthalmology or histopathology findings.

Based on the results of this study, with the assumption that the decrease in survival was the result of vehicle and/or compound aspiration, the no-observed-effect level (NOEL) of m-Xylene was 200 mg/kg/day in the females. However, due to significantly decreased body weight gain in Groups 3 and 4, the NOEL for the males was 100 mg/kg/day.

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INTRODUCTION

The purpose of this study was to evaluate the subchronic toxicity of m-Xylene when administered to rats daily by oral gavage for at least 90 days. The study was conducted according to applicable EPA guidelines and the Good Laboratory Practice regulations.

A copy of the study protocol and all amendments are contained in Appendix 9. The study was initiated on April 11, 1986, and was terminated on July 16, 1987. The study was performed at the Rockville, Maryland, facility of Hazleton Laboratories America, Inc. (HLA).

TEST MATERIAL

The test material, m-Xylene (CAS 108-38-3), Lot No. 259 211, was a clear, colorless liquid. It was received from Fluka Chemical Corporation, Hauppauge, New York, in three shipments (March 6, April 17, and April 30, 1986) and was stored frozen and protected from light. Dosing formulations were prepared using corn oil as the vehicle and were adjusted to 100% activity, based on a purity of 99%. The formulated test material was stored at room temperature.

Analyses for purity, stability, and dose concentration were performed on the test material.

TEST ANIMALS

Sprague-Dawley rats were used in this study because they have historically been used in safety evaluation studies and were requested by the EPA. A total of 168 males and 168 females was received from Charles River Breeding Laboratories, Inc., Portage, Michigan, on March 25, 1986. They were acclimated to laboratory conditions for approximately two weeks, making them 46 days of age at the time of study initiation. The body weights at initiation ranged from 203.7 to 246.4 g for the males and 142.1 to 174.8 g for the females.

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The rats were uniquely identified by ear tags and cage cards and were housed individually in elevated wire-mesh cages. Commercial rodent diet (Purina Certified Rodent Chow® #5002) and acidified tap water were available ad libitum. The temperature and relative humidity in the animal room were recorded twice daily (with few exceptions) and ranged from 70 to 77°F and 31 to 69%, respectively. A 12-hour light/dark cycle was maintained daily via artificial illumination.

METHODS

Groups and Dose Levels

Following physical and ophthalmologic examinations, 85 clinically acceptable rats of each sex were assigned to treatment groups (shown below) using a computer weight randomization program. Animals not selected were assigned to another study or discarded without necropsy. Baseline groups were used for pretreatment bloodwork and later discarded without necropsy.

Group	<u>No. of</u>	Animals	Animal	Numbers	Dose Level
	<u>Males</u>	Females	Males	Females	(mg/kg/day)
<pre>1 (Control) 2 3 4 5 (Baseline)</pre>	20 20 20 20 20 5	20 20 20 20 20 5	8362-8381 8402-8421 8442-8461 8482-8501 8522-8526	8382-8401 8422-8441 8462-8481 8502-8521 8527-8531	0 100 200 800 0

Compound Preparation and Administration

Dosing solutions were prepared weekly according to the following procedure. For each dose level, the calculated amount of test material was weighed and transferred to a volumetric flask. Corn oil was added to achieve the final volume, then the flask was capped and inverted by hand until thoroughly mixed.

The formulated test material was administered to the animals by oral gavage daily for 13 weeks; control animals received the vehicle only. The dosing factor was $2.5\ \text{mL/kg}$.



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Analytical Chemistry

The test material was analyzed for identity and purity prior to initiation of the study and again at termination for purity only. Formulated test material was analyzed for stability and dose concentration. The schedule and results of these analyses are included in the Analytical Chemistry Report (Appendix 9).

Observations and Records

All rats were observed for overt signs of toxicity daily, beginning about one hour after completion of dosing. In addition, a cursory exam was conducted during dosing. Complete physical examinations were performed at initiation and weekly thereafter. Mortality/moribundity checks were performed twice daily. Individual body weights were recorded during the randomization procedure, at initiation, and weekly thereafter. Food consumption was recorded weekly.

Ophthalmoscopic Examinations

Ophthalmoscopic examinations were performed by a board-certified veterinary ophthalmologist on all animals to be used on study prior to treatment and on the last ten survivors per sex per group during Week 13. Pupils of both eyes were dilated prior to examination using 1% Atropine Sulfate.

Clinical Pathology

Clinical pathology determinations (shown below) were made on five animals per sex (Baseline group) prior to initiation and on the first ten survivors per sex per group during Weeks 5^a and 13. Following an overnight fast, samples were collected via the orbital sinus while under carbon dioxide anesthesia.

aprotocol required bloodwork for Week 4 was actually performed during Week 5.



- 12 -

Hematology:

leukocyte count erythrocyte count hemoglobin hematocrit

platelet count differential leukocyte count reticulocyte count cell morphology

Serum Chemistry:

sodium
potassium
chloride
total protein
albumin
calcium
phosphorus
total bilirubin
urea nitrogen

creatinine
glucose
SGOT/AST
SGPT/ALT
globulin
alkaline phosphatase
cholesterol
albumin/globulin ratio
lactate dehydrogenase

Sacrifice and Gross Pathology

All animals that died during the course of the study and all survivors sacrificed after 13 weeks of treatment were given a complete gross necropsy. The method of euthanasia was exsanguination while under sodium pentobarbital anesthesia. The necropsy included examination of the following:

the external surface all orifices cranial cavity carcass external surface of the brain the thoracic, abdominal, and pelvic cavities and their viscera the tissues and organs of the neck region

At the terminal sacrifice, five animals per sex from the control group and 10 animals per sex from each treated group were selected for electron microscopy. A separate report, including methods and results, is to be submitted to the Sponsor by the performing laboratory.



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Organ Weights

For all terminally killed animals, except those selected for electron microscopy, the following organs were weighed. Organ-to-body weight ratios were calculated using each animal's terminal body weight.

liver kidneys spleen adrenal glands brain with stem heart testes with epididymides ovaries

Tissue Preservation

The following tissues from each animal (when present) were preserved in 10% neutral buffered formalin:

all gross lesions brain with brainstem (medulla/pons, cerebellar cortex, and cerebral cortex) pituitary thyroid with parathyroids thymus lungs trachea heart salivary glands (mandibular) liver sternum with bone marrow mammary gland thigh musculature eyes skin epididymides prostate seminal vesicles

kidneys adrenals pancreas testes ovaries uterus spleen aorta esophagus stomach (forestomach and glandular) duodenum, jejunum, ileum colon, cecum, rectum urinary bladder mesenteric lymph node sciatic nerve femur including articular surface cervical spinal cord mid-thoracic spinal cord lumbar spinal cord exorbital lacrimal glands

Histopathology

All preserved tissues from all animals were embedded in paraffin, sectioned, and stained with hematoxylin and eosin.

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The following tissues were examined microscopically:

- (1) All tissues from control and high-dose animals and from all animals not surviving to termination.
- (2) Gross lesions, lungs, liver, and kidneys from all remaining animals.

Statistical Analysis

Cumulative survival data were analyzed using the National Cancer Institute Package (Life Table Analysis). Trend analysis of survival was evaluated at the 5.0% one-tailed probability level.

Body weights, food consumption, appropriate clinical pathology data, and organ weight data from the control group were compared to those of the treated groups of the same sex. Tests for homogeneity of variances and ANOVA were evaluated at the 5.0% one-tailed probability level. Control vs. treated group means were evaluated using Dunnett's t-test at the 5.0% two-tailed probability level.

Data transformations were performed when variances were heterogeneous (see Figure 1) and are indicated in the tables by the appropriate superscript next to the control group mean:

- A = Data analyzed following log_{10} transformation
- B = Data analyzed following square (x^2) transformation
- C = Data analyzed following square root (x $\frac{1}{2}$) transformation
- $D = Data \ analyzed \ following \ reciprocal (1/x) \ transformation$
- E = Data analyzed following angular (arcsine $x^{1/2}$) transformation
- F = Data analyzed following rank transformation



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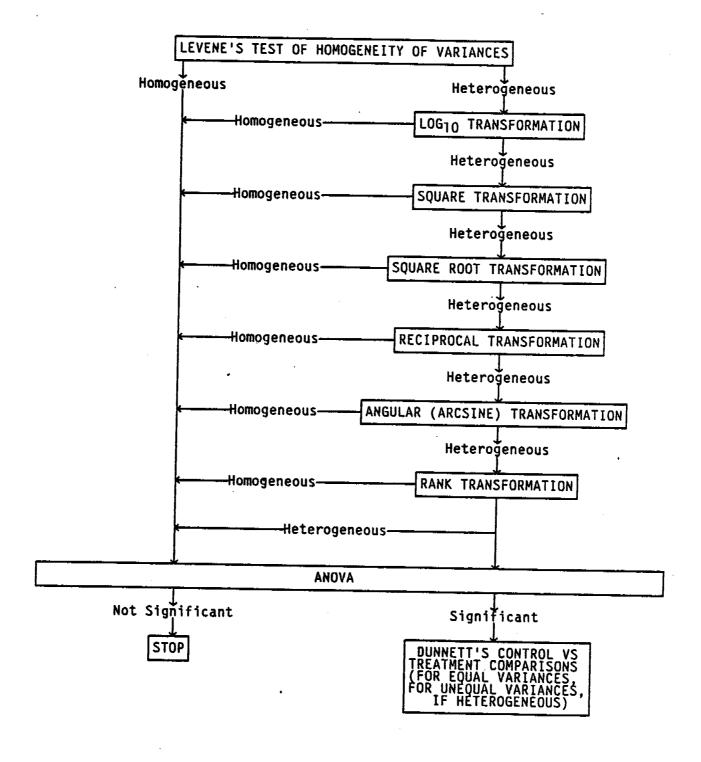
Throughout this report, when an effect is referred to as "significant", it means there is a statistically significant difference between the control group and the specified treated group of the same sex. Statistical significance is indicated in the tables by an "s" superscript next to the treated group mean.

Raw Data and Final Report Storage

All raw data and the final report are stored in the archives of Hazleton Laboratories America, Inc.

FLOWCHART OF ANOVA AND RELATED METHODS

FIGURE 1





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RESULTS

Mortality

Group survival data, by week of study, are presented in Table 1. Individual animal disposition is presented in Appendix 1.

In the males, there was significantly higher mortality in Group 3, but there was not a significant trend. In the females, there was significantly higher mortality in Groups 3 and 4 and there was a significant trend.

Clinical Signs

A summary incidence of weekly clinical signs is presented in Table 2; individual data are presented in Appendix 2. A summary incidence of daily observations is presented in Table 3 (signs with only a single occurrence are not included).

The most commonly observed weekly clinical signs were chromodacryor-rhea, malocculusion, and urine stains. Of the signs recorded, only urine stains showed a possible relationship to treatment: it was seen only in both sexes of Group 4.

Daily observations included hyperactivity, convulsions, salivation, and epistaxis. Except for salivation, these were observed only during the first three weeks of the study and with low frequency. Salivation was observed in both sexes of Group 4 during almost every study week, with the incidence considerably higher in the females. Generally, salivation was observed just prior to dosing and the animals were back to normal by the one-hour post-dosing observations.

Body Weights and Food Consumption

Mean body weights are presented in Tables 4A (Mean Body Weights), 4B (Body Weight Change) and graphically in Figure 2; individual values are



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presented in Appendix 3. Food consumption data are presented in Tables 5A (Weekly Mean Values), 5B (Total Food Consumption at Selected Intervals) and graphically in Figure 3; individual values are presented in Appendix 4.

The mean body weight gain over the course of the study was significantly decreased in Groups 3 and 4 of the males and in Group 4 of the females. The body weight curves in Figure 2 show a clear relationship between dose and body weight depression in both sexes.

Statistical analyses were performed on food consumption data for three intervals: Weeks 1-5, 6-9, and 10-13. Food consumption was significantly decreased from Weeks 1 to 5 in the Group 4 males and from Weeks 6 to 9 in the Groups 3 and 4 males. Food consumption data among the female groups was comparable at all three intervals.

Ophthalmoscopic Examinations

Individual ophthalmoscopic findings and copies of the ophthalmologist's reports are presented in Appendix 5.

Only two animals (one Group 1 male and one Group 3 male) showed abnormalities at the terminal examination. These were judged to be unrelated to treatment.

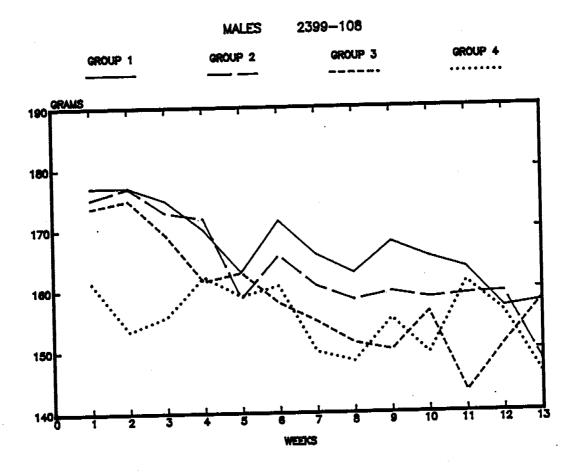
Clinical Pathology

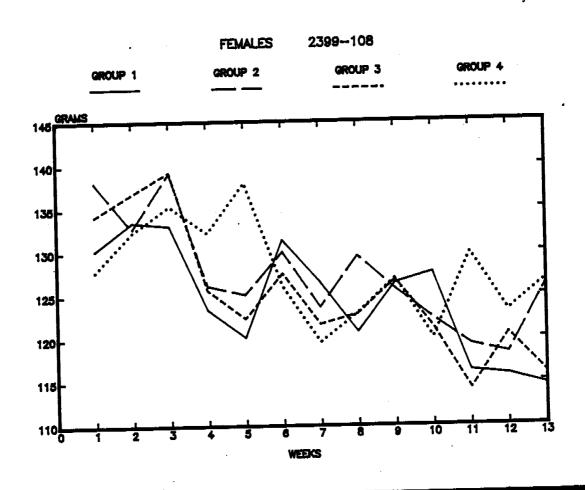
Mean hematology values are presented in Table 6; individual values are presented in Appendix 6. Mean clinical chemistry values are presented in Table 7; individual values are presented in Appendix 7.

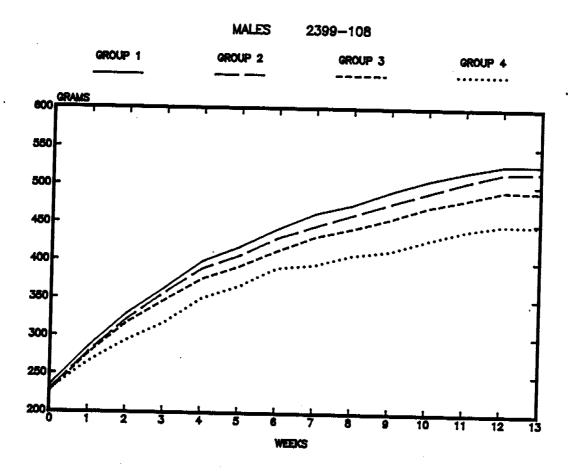
At the Week 5 interval, only one hematology parameter was significantly different: hematocrit was decreased in Group 4 females. At Week 13, there were no significant changes in the hematology values of either sex.

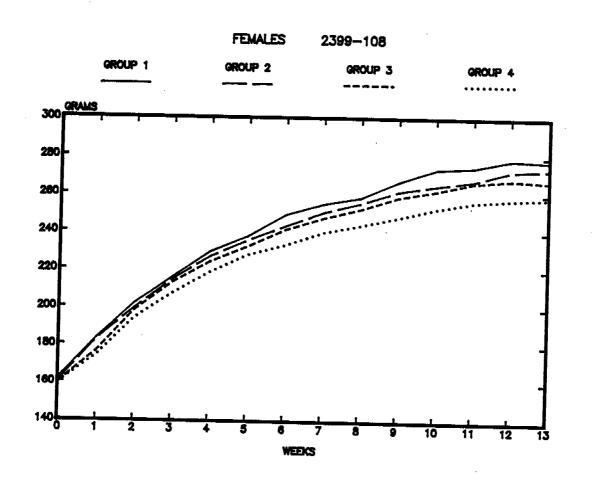
There were significant changes in a few of the clinical chemistry parameters at the Week 5 interval. In Group 4 males, potassium was increased and total bilirubin was decreased. In the females, cholesterol and calcium

FIGURE 3 - MEAN FOOD CONSUMPTION











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were increased in Group 4 and potassium was increased in Groups 3 and 4. There were fewer significant changes at Week 13: alanine aminotransferase was increased in Group 4 males, and calcium and cholesterol were increased in Group 4 females.

Organ Weights and Organ-to-Body Weight Ratios

Mean organ weights (absolute) and organ-to-body weight ratios (relative) are presented in Tables 8 and 9, respectively; individual values are presented in Appendix 8.

The terminal body weight in Group 4 of both sexes was significantly decreased. In the males, there were a few significant changes in organ weights, all in Group 4: heart weight was decreased and relative brain and relative kidney weights were increased. In the females, there were no significant changes in absolute or relative organ weights.

Gross Pathology

Gross pathology incidence summaries are presented in Tables 10A (Terminal Sacrifice) and 10B (Unscheduled Deaths); individual gross observations are presented in Appendix 8.

There were few gross lesions observed in this study. The most commonly seen were mottled lungs and failure of the lungs to collapse. Both were observed most frequently in Groups 3 and 4 of both sexes. The other lesions observed were sporadic and showed no apparent dose relationship.

Histopathology

Histopathology incidence summaries are presented in Tables 11A (Terminal Sacrifice) and 11B (Unscheduled Deaths); individual data are presented in Appendix 8. Evaluation of microscopic findings is included in the Pathology Summary.



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In the animals examined at the terminal sacrifice, a variety of spontaneously occurring incidental lesions were observed, none being related to treatment. In the 19 unscheduled deaths, all but one of the animals had foreign material in the alveoli. These deaths were judged to be related to gavage dosing accidents and not to the test material.

Analytical Chemistry

Analytical chemistry methods and results are included as Appendix 9.

Stability data showed there was little loss of test material after 21 days of storage at room temperature or 5°C refrigeration. Dose verification analyses showed that all samples analyzed were within the specified limits (±10% of target concentration).



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DISCUSSION

Xylene (mixed) is a mixture of m-Xylene, p-Xylene, o-Xylene, and ethylbenzene. The exact proportion is variable and depends on the material (petroleum or coal tar) from which it is produced. In this study the m-xylene (99% purity) was tested. In previous studies with xylene (mixed) conducted by the NTP in rats, deaths were noted at 4,000 and 6,000 mg/kg in a single dose study and at 2,000 mg/kg in a 14-day study. In the 13-week study all rats at dose levels up to 1,000 mg/kg survived to termination. Also, mean body weights were 15% and 8% lower than control in the males and females, respectively, no signs of clinical toxicity were observed, and no compound-related gross or microscopic lesions were observed. In a 2-year study, males dosed at 1,000 mg/kg has a slightly higher mortality rate than did the vehicle controls, but the number of gavage deaths was also higher. It was postulated that the dosed males resisted gavaging because of the xylenes. In the 2-year study, no nonneoplastic or neoplastic lesions resulted from exposure to xylene (mixed).

In this 90-day study conducted with the m-Xylene isomer, mortality was significantly increased in Group 3 males and Groups 3 and 4 females, the incidence of salivation was increased in Group 4 males and females, body weight gain was decreased in Groups 3 and 4 males and Group 4 females, food consumption was decreased in Group 4, and several changes were noted in clinical pathology and organ weight data. Histopathology revealed no compound-related changes. The deaths in the treated groups are most likely the result of vehicle/test material aspiration since there was no physical evidence of trauma (perforated trachea and/or esophagus) and the low vapor pressure of xylene (about 10 mm Hg at 28°C). Although the findings in this study suggest m-xylene is slightly more toxic than xylene (mixed), these findings are generally consistent with those noted by the NTP using xylene (mixed).



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Based on the results of this study, with the assumption of vehicle and/or test material aspiration producing the deaths in the treated animals, the no-observed-effect-level (NOEL) of m-xylene was 100~mg/kg/day in the males and 200~mg/kg/day in the females.

Study Director

Study Coordinator

Gary W. Wolfe, Ph.D., D.A.B.T.

Patrick M. Vanatta, B.S.

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PATHOLOGY SUMMARY

Subchronic Toxicity Study in Rats with m-Xylene

General Protocol

Eighty male and 80 female Sprague-Dawley/Charles River rats were randomly divided into groups of 20 males and 20 females each. Groups were assigned to study according to the following schedule:

Group Number	<u>Number o</u>	f Animals	Dosage Levels
	<u>Male</u>	Female	mg/kg/day
<pre>1 (Control) 2 (Low) 3 (Mid) 4 (High)</pre>	20	20	0
	20	20	100
	20	20	200
	20	20	800

The test material was administered by oral gavage, 7 days per week for 13 weeks. Treatment was continued until the day before necropsy. At termination, all surviving animals were killed and necropsied. Tissues were preserved in formalin. Complete tissues, as outlined in the protocol, were examined microscopically from all control and high dose animals and also from all animals not surviving to termination. Gross lesions, lung, liver and kidney were examined from all remaining animals. The following is a summary of histologic findings.

<u>Histopathology</u>

Scheduled Deaths

No treatment-related lesions were observed in animals receiving m-Xylene for 13 weeks. A variety of spontaneously occurring incidental lesions were observed and these were of the type and frequency expected in



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this strain and age of rat. The most commonly observed changes included perivascular/peribronchiolar lymphoid infiltrates in the lung, degenerative cardiomyopathy, foci of mononuclear cells and bile duct inflammation in the liver, chronic progressive nephropathy, chronic inflammation of the Harderian gland, and dilation of the uterus. A low dose female was observed to have a mammary adenocarcinoma. This is an uncommon, but not rare, neoplasm and although it is unusual to observe this in an animal of this age, it is considered to be spontaneous and not related to intake of the test material.

Unscheduled Deaths

Four females and two males from Group 4, five animals of each sex from Group 3 and three males from Group 2 died or were killed moribund on study. The majority of these animals which died on study had foreign material in alveoli. Usually this material elicited little or no inflammatory response although one high dose male developed foreign body pneumonia. This material was transparent and globular but nonrefractile and is felt to be compound and/or vehicle. These deaths are considered to be related to gavage accidents.

Conclusion

Administration of m-Xylene for 13 weeks to male and female rats did not result in treatment-related histomorphologic alterations. Experimental deaths are considered to be related to gavage accidents.

Pathologist:

Borge M. Ulland, D.V.M.

Diplomate, American College of Veterinary Pathologists

Life Sciences Division

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REFERENCES



- 28 -

<u>Hematology</u>

Erythrocyte Count (RBC)

- Coulter Electronics, Inc. Coulter Counter Model S+II System, product reference manual 4235052C. Hialeah, FL: Coulter Electronics, Inc.; 1982 February.
- Coulter Electronics, Inc. Coulter Counter Model S+IV System, product reference manual 4235328C. Hialeah, FL: Coulter Electronics, Inc.; 1986 April.

Hematocrit (HCT)

- Coulter Electronics, Inc. Coulter Counter Model S+II System, product reference manual 4235052C. Hialeah, FL: Coulter Electronics, Inc.; 1982 February.
- Coulter Electronics, Inc. Coulter Counter Model S+IV System, product reference manual 4235328C. Hialeah, FL: Coulter Electronics, Inc.; 1986 April.

Hemoglobin (HGB)

- Coulter Electronics, Inc. Coulter Counter Model S+II System, product reference manual 4235052C. Hialeah, FL: Coulter Electronics, Inc.; 1982 February.
- Coulter Electronics, Inc. Coulter Counter Model S+IV System, product reference manual 4235328C. Hialeah, FL: Coulter Electronics, Inc.; 1986 April.

Leukocyte Count (WBC)

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Alanine Aminotransferase (ALT) - CentrifiChem®

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Albumin (ALBUMIN) - CentrifiChem®

Baker Instruments Corporation. Baker™ Instruments CentrifiChem® Albumin insert #RD700-0. Allentown, PA: Baker Instruments Corporation; 1984 March.

Albumin/Globulin Ratio (A/G RATIO)

Albumin E Globulin = A/G Ratio (Calculated).

Alkaline Phosphatase (ALK P) - CentrifiChem®

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Aspartate Aminotransferase (AST) - CentrifiChem®

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<u>Calcium (CALCIUM) - CentrifiChem</u>® .

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Chloride (CHLORIDE) - Beckman System E4A™ Electrolyte Analyzer

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Creatinine (CREAT) - CentrifiChem®

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Globulin (GLOBULIN)

Total Protein - Albumin = Globulin (Calculated).

Glucose (GLUCOSE) - CentrifiChem®

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Sodium (SODIUM) - Beckman System E4A Electrolyte Analyzer

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Total Bilirubin (T BILI) - CentrifiChem®

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Sclavo® Inc. Instrument Application CentrifiChem 500/600 Series Total Bilirubin #32F1082. Wayne, NJ: Sclavo Inc.

Total Cholesterol (T CHOL) - CentrifiChem®

Baker Instruments Corporation. Baker™ Instruments CentrifiChem® Cholesterol Reagent - 6 min. insert #RD576. Allentown, PA: Baker Instruments Corporation; 1983 January.

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Baker Instruments Corporation. Baker™ Instruments CentrifiChem® Cholesterol Calibration Standards insert #27726812. Allentown, PA: Baker Instruments Corporation; 1983 February.

Total Protein (T PROT) - CentrifiChem®

Baker Instruments Corporation. Baker™ Instruments CentrifiChem® Total Protein insert #RD712-0. Allentown, PA: Baker Instruments Corporation; 1984 June.

<u> Urea Nitrogen (BUN) - CentrifiChem®</u>

Baker Instruments Corporation. Baker™ Instruments CentrifiChem® BUN insert #27714911. Allentown, PA: Baker Instruments Corporation; 1982 December.

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RANDOMIZATION

Bartlett's Test

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Thomas, D.G.; Breslow, N.; Gart, J.J. Trend and homogeneity analysis of proportions and life table data. Comput. Biomed. Res. 10:373-381; 1977.

TABLE 1 ADJUSTED SURVIVAL

							WEEK							
GROUP	0	П	2	က	4	2	9	7	∞	6	10	17	12	13
Male														
, .	20/20	20/20	20/20 20/20 20/20 20/20	20/20	20/20	20/20	20/20	20/20	20/20	20/20	20/20	20/20	20/20	20/20
2	20/20	20/20	20/20 19/20	18/20	18/20	17/20	17/20	17/20	17/20	17/20	17/20	17/20	17/20	17/20
က	20/20	19/20	19/20	17/20	17/20	16/20	16/20	16/20	15/20	15/20	15/20	15/20	15/20	15/20
4	20/20	20/20	20/20	19/20	19/20	19/20	19/20	19/20	18/20	18/20	18/20	18/20	18/20	18/20
Female													*	
-	20/20	20/20	20/20	20/20	20/20	20/20	20/20	20/20	20/20	20/20	20/20	20/20	20/20	20/20
2	20/20	20/20	20/20	20/20	20/20	20/20	20/20	20/20	20/20	20/20	20/20	20/20	20/20	20/20
æ	20/20	20/20	18/20	17/20	17/20	17/20	17/20	17/20	17/20	17/20	17/20	17/20	17/20	16/20
4	20/20	20/20	18/20	18/20	18/20	18/20	18/20	17/20	17/20	17/20	17/20	16/20	16/20	16/20

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TABLE 2

a Total incidence for entire study.

TABLE 3 INCIDENCE OF DAILY OBSERVATIONS^A (Weekly Totals by Sex and Group)

Incidence of Convulsions

4	14~		ı	ı	ı	1		•			
	13		1	ı	1	1		ı	1	1	1
	12		ı	ı	1	ı		ı	1	į	1
	11		ı	1	ı	1		ı	I	i	ı
	10		1	ı	•	ı			ı	ı	1
	6		ı	ı	1	ı		ı	ı	ŧ	4
	8		t.	ı	ı	ı		ı	ı	ı	1
WEEK	7		ı	ı	1	1		1	ı	i	ı
	9		ı	ı		ı		ı	ı	ı	1
	2		ı	ı	ı	ı		1	1	ı	ı
	4		1,	•		1		ı	1	1	ı
	3		1	1/19	ı	1/20		1	•	ı	1
	2		ı	•	1	ŧ		i	•		2/20
	1		1	ı	1	ı		1	ı	1	ı
	GROUP	Male	, , ,	2	င	4	Female	-	2	ო	4

^aNumber of observations during week/number of survivors in group at beginning of week. Dash indicates bno incidence during week. Partial week (terminal sacrifice)

TABLE 3

INCIDENCE OF DAILY OBSERVATIONS^a (Weekly Totals by Sex and Group)

Incidence of Hyperactivity

	14		1	1	,	ı		ı	1		1	
	13		r	ı	1			1	ı		1	
											•	
	12		1		,	1			ŧ	1	1	
	11		ı	1	1	Í	٠	1	i	1	1	
	10		ı	ı	ı	ı		í	ı	ı	1	
	6		1	1	ı	ı		1	1	ı	1	
	8		1	ı	ı	ı		1	ı	1	ı	
WEEK	7		ı	ı	ı	t		ı	ı	ı	ı	
	9		ı		ı	1		ı	ı	1	ı	
	5		١.	1	ı	ı		ı	1	1	1	
	4		ı	ı	1	ı		1	ı	ı	ı	
	e		ı	ŧ	ı	ı		1	ı	ı	ı	
	2	٠.	ı	1	ì	1		1	ı	3/19	2/20	
,	-		ı	ı	ı	ı		·	1	1	ı	
411000	מאסטא	Male		2	က	4	Female		2	က	4 - 2/20	

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^aNumber of observations during week/number of survivors in group at beginning of week. Dash indicates bno incidence during week. Partial week (terminal sacrifice)

TABLE 3 INCIDENCE OF DAILY OBSERVATIONS^a (Weekly Totals by Sex and Group)

Incidence of Epistaxis

							MEEK							4
GROUP 1 2	1	2 3	3	4	5	9	7	8	6	01	11	12	13	14
Male		•												
-	ı	ı	1	i	•	ı	ı	1	ı	ŧ		ı	ı	ı
2	ı	ı	1	ı	1	•	í	ı	1		1	ı	,	ı
æ	i	1	ı	ı	1	ı	ı	í			1	ı	i	1
4	ı	2/20		ı	ı		1	1	1	ı	ı	ı	ı	
Female	٠									,		•		
	ı	1	1	ı	1	1	1	ı	1	ı	1	1	ı	ı
7	1	1/20	ı	1	ı	•	1	1	1	ı	•	i	· 1	1
т	1	ŧ	1	ı	ı	i	1		1	1	ı	ı	1	1
4	1/20	3/20	1	ŧ	1	ı	1	1	· · ·	1	ı	ı	i	1

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^aNumber of observations during week/number of survivors in group at beginning of week. Dash indicates no incidence during week.

^bPartial week (terminal sacrifice)

TABLE 3
INCIDENCE OF DAILY OBSERVATIONS^a
(Weekly Totals by Sex and Group)

Incidence of Salivation

WEEK 7 7 19 7/19															
	<u>م</u>	-	2	3	4	2	9	NEEK 7	8	6	10	11	12	13	14 ^b
	a) l													-	
		1	1	ı	ı	1	ı	ı	ı	ı	•	•	•	ı	ı
		1	ı	ı	ı	1	1	•	ı	•	ı	ı	ı	ı	ı
- 16/20 14/20 11/19 2/19 8/19 7/19		ı	ı		i	ı	ı	ı	. •	1	ı	ı	1	· 1	ı
			16/20	14/20	11/19	2/19	8/19	7/19	1/19	4/18	2/18	2/18	ı	1/18	ı
48/18 38/18	ale														
48/18 38/18		1	1	1	•	•	ı	ı	ı	ı		ı	1	ı	1
48/18 38/18		ı	1/20	ı	1	ı	ı	J	•	ı	t	i	ı	ı	ŧ
48/18 38/18	•	,		1/18	. • ¹	ł	ı	1	•	ı	1/17		1	ı	ł
•		6/20	39/20	46/18	50/18		48/18	38/18	29/17	25/17	22/17	20/16	25/16	28/16	10/16

^aNumber of observations during week/number of survivors in group at beginning of week. Dash indicates bno incidence during week. Partial week (terminal sacrifice)

TABLE 4A MEIGHTS AND STANDARD DEVIATIONS (G) SUBCHRONIC TOXICITY IN RATS

GROUP AND DOSE LEVEL (MG/KG)	WEEK:	WEEK: START		2	m	4	ی	9	7	CS !	6	10	11.	12	13
1	!	1 1 1		 			MALES								
e4	MEAN S.D.	234.5 6.84	284.8 9.72	328.6 13.52	362.8 18.35	398.4 22.92 20	418.1 26.60 20	442.1 28.79 20	462.4 29.51 20	474.2 31.81 20	491.8 34.54 20	506.5 36.57 20	517.8 41.09 20		527.8 46.28 20
. 000	MEAN S.D.			21.18 21.28 19	356.5 22.24 18	388.8 24.91 18	406.5 24.17 17	430.0 26.70 17	445.9 32.01 17	461.0 .32.69 17	476.1 35.44 17	490.4 35.26 17	504.7 38.46 17	516.9 37.79 17	518.1 37.55 17
3	MEAN S.D.	226.9 10.40			346.8 16.02 17	375.5 19.19 17	392.1 25.01 16	413.2 25.13 16	431.8 24.73 16	443.1 25.72 15	456.1 24.40 15	471.5 24.24 15	481.7 23.26 15	493.2 25.57 15	492.1 31.26 15
200.000 4 4 800.000	MEAN S.O.		265.1 17.74 20	293.4 24.28 20		349.8 20.98 19	366.5 24.71 19	390.2 23.73 19	394.8 26.07 19	407.7 26.32 18	413.6 27.98 18	428.1 25.85 18	441.0 27.34 18	448.8 33.47 18	448.1 30.37 18
							FEMALES					,			
1	MEAN S.D.	162.0 5.34 20	183.4 7.79 20	201.8 8.99 20	215.7 11.59 20	229.3 14.16 20	237.5 15.89 20	249.1 19.62 20	254.9 20.25 20	258.4 21.41 20	267.0 19.46 20	273.5 22.49 20	274.8 20.34 20	278.8 20.74 20	277.9 19.81 20
2	MEAN S.D.				214.4 10.14 20	226.7 10.33 20	235.4 11.43 28	243.1 11.36 20	250.4 13.17 20	255.4 11.69 20	261.7 12.29 20	264.9 12.35 20	267.5 14.08 20	272.8 16.10 20	273.7 15.32 20
3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3	MEAN S.D.					223.9 15.20 17	232.2 12.80 17	241.2 12.25 17	247.4 16.04 17	252.3 13.72 17		262.2 14.84 17	266.6 16.59 17	268.3 17.08 17	267.2 17.20 16
4 800.000	MEAN S.D.				207.2 14.57 18	218.4 13.04 18	227.7 14.71 18	233.0 16.41 18	239.7 15.13 17	243.6 15.28 17	248.1 13.96 17	252.6 14.51 17	256.3 13.56 16	257.8 15.89 16	258.6 18.42 16

HLA 2399108

105.Ft 450	800Y WEIGHT CHAN	TOXICITY IN RATS
		SUBCHRONIC

		n - 13
GROUP AND	OOSE LEVEL	(MG/KG)

WEEK

MALES

293.3	289.5	265.2	219.5
43.46	30.61	30.37	26.16
20	17	15	18
MEAN	MEAN	MEAN	S.O.
S.D.	S.D.	S.D.	
1	2	3	4
. 000	100.000	200.000	

115.9	18.00 20
MEAN	S.D.
₹	000.

FEMALES

115.9 18.00	20	113.2	20	107.2	14.36 16	98.1	16.21 16
MERN S.D.	z	MERN	; ; z	MEAN	i Z	NERN	S.D.
- -1	000.	2	100.000	ĸ	200.000	.4	800.000

2399108

HLA

TABLE 5A MEAN FOOD CONSUMPTION AND STANDARD DEVIATIONS (G/WK) SUBCHRONIC TOXICITY IN RATS

GROUP AND DOSE LEVEL	LEFE FER	~	2	۳n	4	r	•	^	C	٥	10	11	12	13'
NOW YOUR			1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1		1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	1						
							MALES							
	MEAN	177.0	177.0	174.8	170.0	162.9	171.4	165.8 13.19	162.8 12.96	167.8 13.88	165.3 13.89	163.5 15.94	156.9 17.93	157.8 13.89
000.	o S S	14.88 20	16.53 20	12.70 20	20	10						19	9Z	0 1
8	HE PA	175.1	176.9	172.8	171.8	158.6 8.52	165.7 13.54	160.6 15.84	158.3 10.99	159.6 12.04	158.6 9.66	$\frac{159.1}{11.00}$	159.4 9.44 17	148.2 12.11 7
100.000	i z	20	18	17	18	^						9		•
'n	ME AN	173.6	174.9	169.1	161.5 15.22	162.8 4.05	157.8 10.25	154.8 7.30	151.2 10.28	150.0 9.84	156.3 9.80	143.1 18.26 11	150.9 14.41 15	158.1 17.92 5
200.000	i n z	19.00	19	17		9		15	15					
4		161.3	153.3	155.7	162.2	159.0 16.39	160.7 13.89	149.8 15.20	148.2 19.03	155.2 17.29	149.4 11.85	161.2 20.29	156.2 21.78	146.U 17.78 8
800.000	ń z	20	20	19		6		16	15	91				•
•							FEMALES							
-					123.4	120.1	131.4	126.5	120.7	126.3	127.6	116.2	115.7	114.5 9.86
•	0 2	10.52	13.03	10.13 17	13.77 18	13.65 10	14.71 19	19.20	16.71	19.27	18	15	20	16
	2 2				126.1	125.1	130.0	123.6	129.5	125.6	122.3	119.2	118.2	126.1 31.06
7	S.D.	14.39	11.28	11.74	11.58	14.13	14.43	11.42 19	22.02 19	15. 19 19	20	18	19	6
100.000	z				0.7			•	6	107	191 3	114.1	120,5	116.0
m	MEAN	134.2	136.8	139.3	125.6	122.3	127.5 13.61	121.6	18.59	17.78	11.65	12.25	19.88	11.83 6
200.000	i z	19			16			15	2	9	` '	2 6		7 761
4	MEAN		132.3	135.3	132.2	138.0 19.55	126.0 24.63	119.6 8.35	122.9	126.9	120.0 14.15	24.37	18.17	19.65
800.000	o z				13		17	12	4	12	†	ţ	2	ı

MEAN TOTAL FOUD CONSUMPTION AND STANDARD DEVIATIONS (G)

(9)																		
SUBCHRONIC TOXICITY IN RATS	ыЕЕК 10 - 13	MALES	0444.3 7	92.29	6:11.6	34.33 6	44	23.15		28.92 5	77	472.4	28.32 9	478.0	52.80 8	455.6	40.62 6	488.8 43.20 ó
IC TOXICIT	9	Ä	667.8	248.31	640.6	14	611.7	30.73	612.0	55.08 14	FERV	511.4	46.89	505.4	48.52	493.4	50.78 15	479.7 33.23 10
SUBCHRON	1 - 5		860.0 44.03	10	831.4	, o	849.5	25.81 6	273.6	59.64 8		634.9	56.91 8	650.1	56.50 9	678.9	5	656.8 46.35 5
	· ,		MEAN	i i z	MERN	; ; ; z	MERN	o o z	MEAN	S.D.		MEAN.	i z	AE D	i i z	MERN	. z	S.D.
	GROUP AND DOSE LEVEL (MG/KG)		; ⊣	. 000	2	100.000	'n	200.000	4	800.000		+=1 ,	000.	5	100.000	٣	200.000	4 800.000

FORTE 6 SUBCHES OF THE FOLKS SUBCHESION OF THE ROLS SUBCHESION TO THE ROLS

GROUP AND			Res ntzall		Ħ			<u>=</u>	1.1	*	PLAIELET.	ELET THAME.	•
DOSAGE LEUFL		* *		* * 1 1 1 1 1 1 1 1 1			k #		4	*	; ; ; ; ; ; ; ; ; ; ; ; ; ; ; ; ; ; ;		*
							ž	пн. Е					
1 0 MG/KG	HERN S.D.		7.66 .671	8.47 .262 10		15.6 .72 10	15.7 .38		43.8 3.83	43.4 1.41 10		392.3 10	1181 195.9 10
2 100 M37KG	MEAN S.D.	· .	7.66 .507 10	8.50 .362 10		15.5 .2.7 10	15.8 .23 11		44.4 2.60 10	2.11 2.11 18		1209 145.0 18	1113 125.4 10
3 200 MG/KG	MERN S.D.		7.83 .288 10	8.59 374 10		15.5 .56 10	15.7 .62 10		44.5 1.78	44.0 1.4.7 10		1241 119.0 10	1156 119. n 10
4 800 MISZKG	MEAN S.D.		7.53 .497 10	8.51 .827 10		15.6 .6.7 10	15.7 1.59		42.7 2.68 110	43.9 4.26 18		1194 91.4 9	1103 126.4 11
9 RASELINE	MEAN 9.D.	5.48 .752			14.9 77.			34.4 5.4.8 8			1193 226.4 5		
						٠	1111	FEMALE					
1 0 MG/KG	MEAN S.D.		7.05 .704 10	9.15 .256 10		15.1 .57 10	15.5 69. 10		40.1 4.16	43.6 1.67		1225 69.2 18	1142 132.0 10
2 100 MG/KG	S.D.		6.96 629 10	8.13 .268 18	·	15.4 .45	15.7 .eq		40.0 4.04 10	43.6 1.28 10		1317 116.2 18	1156 121.9
3 200 MGZKG	MEAN S.D.		6.94 6.50 1.030	8.23 .2911 111		15.4 .26 10	15.8 .e.s		39.9 3.62 18	44.2 1.40 E		1276 132.1 111	1184 212.1 10
4 840 MG/KG	MEAN S.D. N		6.42 .950	8.08 .36. .36.		15.3 .64	15.4 HH		36.0 8 2.28 10	42.8 2.3 n n n n		1247 Jinu. 1 Jin	1164 118. n
5 ВАSEL1NE	MEAN S.D. N	4.5. 42.6. 8			15.2 .48			28.6			1352 85.8 8		,

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FABLE 6 - CONTRIBED MEAN DUNICAL HERATOLOGY VALUES STRICHROWLL TOXICLY STROY IN RATS

5 1.5	mai E	.10 .08 D	•		.12 .11			. 053 . 101 10 10 10		.018 .065 Ju 10		FETRALE	.00	, 029 , 052 10 10	. 10	1859 . 455. 10 III	60. 20.	. 016 . 064 16 18	.08 .10	02 87
13 -1		e. 6.	J. J.	:	1.3	10	1.5	1.19 10	1.2	. 28 10	. 26 . 1182 5		1.0	.69	1.1	. 92 10	1.2	. 78 1 n	1.2	=
*		1.3	.67	PT .	1.6	10	1.0	10	1.4	10	7.4 8.		1.0 A	. 38 10	1.4	98. 01	1.0	10	1.3	11
		MEAN	o vi z	:	S.D.	z	MEAN	i i i	MEAN		MEAN S.D.		MEAN	o. z	MEAN	ა Հ	MEAN	ი	MEAN S.D.	z
LEUEL			U FIGZKS		2 100 MG/KG		1 000		4. 000 0		HASEL INE			1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1		100 M5/KG		ZHU MISZKG	4 PN BNO MGZKG 9	

FARM CLIFFECH HETEOPETRY VALUES SUBCHRUITE FEATURY STUDY IN RATS

GREEN PROPERTY.		=	HER FRZUL	F	Œ Æ	B 651 THZBL \$1	- >•		6 FH7ULOS	ű.	(3F 145)	add) THATE(\$)	7
DOSAGE		t	till FK	* * * * *	* *		* * 1 1 1 1 1	F .	6	* 1 1 % 1 1 m 1	- 1	40	*
1 1 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5		i 1 2 1 1 1 1	1 1 1 1 :	; 			<u>=</u>	пел.Е			Ť		
	MF AN		16.3	16.3		•	•		e .	•		.	0.
O MGZKG	.0.5 2		3.48	3.36		9. 3. 3. 3.	= = = =		00°.	<u> </u>		9 -	==
•	:		. K			=	•		•	•		0.	0.
2 100 MG/KG	S.D.		3.49	3.71		. .	; ₹ :		99.	00.7		£n. 00	Ea. ⊒
	z		1.0	10		3 .	=		3	=		; •	·
i s	MEAN		18.4	17.3		٠.	•		•	e. 6		•	• 3
200 MG/KG	.0.8 M		5.34	4.02 10		# <u>9</u>	9 2. 1.		99. 01.			. .	
,	: }			7 71		•	•		•	•		9,	٠.
800 1137KG	S.D.		4.41	4.56		. 55	. 3 <u>.</u>		<u> </u>	0.1		. 0. 10.	Ē. E
	z		10	2		0.4	9		2	3			
э НӨБЕГ 1 үЕ	MEAN S.D.	13.2 3.01						e . Ē. s			9 .00	•	
							FEE	FENDALE					
-	ME DA		14.0	11.8		.	0,		•	٥.		•	e. 0.
0 MGZKG	9.0°		3.68	1,76		## . T	를 <u>-</u>		80. 1.	. E		Î.E	. .
	=		2	:			c		•	¢		-	
2	X 0		13.8	12.6 2.63		no.	, =		; <u>=</u>	: =		93.	ξħ.
1.00 1.05 7.05	i i z		96	1.0		1	16		2	=		Ξ	Ξ
•	MODM	,	4	12.3		0.	•		9.	₽.		•	٠.
200 MG/KG	9.D.		3.40	3.53		(in)	≣.		# C :	E :		£ = 1	≣ ⊆
	z		0.1	0 1		Ξ	=		=	=		2	
*	NOTA		14.9	13.7		•	₽.		٥.	•		•	0.
800 MSZKG			98.3 98.1	5,32		<u>=</u> =	===		Ξ.Ξ.	2 Ξ		= = = - 1	9 9 9 1
80.00 80.00 80.00	MEAN S.D.	15.4 2.51			e			•			• = 3		
	z	ñ.			<u>ئ</u> .			u.			r		

TAME 6 - CONTHINED MEAN CLINICAL HEMATOLOGY VALUES SUBCHROWIC TOXICTLY STUDY IN RATS

The Residue				2	13		ن ا ا	£ 1		2	£ .	7	S	51
								E	F.E.	† † † † † † † † † † † † † † † † † † †	h 1 1 1 1 1	; ! ! ! !	i i i i i i i i i i i i i i i i i i i	! ! !
No.	1			2.6	2.5		13.5	13.6		Τ,	-		-	•
	U Ms/Kb			1.91	1.10		3.74	2.92		.13	.13	-		. ₹
		:		•	3		2	=		::	10		Ē	Ξ
	2 00 00	TES.		1.9	2.4	•	13.8	12.0			-		•	Ī
	I U.D. I POZNAGO	oʻz		æ	2.23		3.45	2.75			.03		.20	•
		:		7	0.7		37	<u>.</u>		1 0	3.6		10	10
No.	5	MERN		5.6	2.7		15.4	14.2		2.	-		c	c
Name	0.0 Mb/Kb			1.42	1.82		5.16	. 2.70		.20	: T		7.	•
		z		≘	<u>-</u>		3.0	36		n (10		9.0	Ξ:Ξ
No. 1.55 1.48 3.66 4.21 1.19 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1	4	MEAN		2.5	2.4		14.3	14.0		c	-		P	,
HEAN 18 110 10 11 10 10 10 1	DB MGZKG	S.D.		1.55	1.48		3.66	4.21		• •	<u>.</u> =		. :	· ·
Fight Figh		z		n.	0.1		=	0.7		, n.	=		10	;
FETTINE FETTINE FETTINE FETTINE FETTINE FETTINE FETTINE FETTINE TA TA<	ιν <u>1</u>	ME'SN	æ;			11.9			4.			-		
FEIRITE FEIR	<u>-</u>	i z	ÿĸ			2. 2. 2. 2. 2. 2. 2. 2. 2. 2. 2. 2. 2. 2			si n a					
GAKG S.D. B. HEAN I. 2.2 B. 1.5 B. 9.8 B. 11.5 B. 9.8 B. 11.5 B. 9.8 B. 11.5 B. 12.2 B. 11.5 B. 11.5 B								FEI	AI E					
SYKG S.D. 1.84 1.76 3.45 1.84 1.16 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10 1.10	1 0 Min 200	HE BN		2.2	1.8		11.5	9.8		úq ,	-		-	-
FEAN 1.9 2.1 11.5 10.2 .	514 Sill 0	. z		. 84 10	. 76 10		3.45 10	1.84		= =	<u>=</u> :		<u> </u>	
STATE 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.0 1.	·	MCON		•)		:	<u>.</u>		2	Ξ
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HEAN 1.8 1.6 12.2 10.5 .1 .0 .2 6.KG 5.D. .68 1.06 3.41 2.28 .14 .0 .2 6/KG 5.D. .78 1.73 13.0 10.7 .2 .1 .1 6/KG 5.D. .78 1.73 2.81 3.30 .2 .1 .18 N IB IB IB IB IB IB IB NGAR 1.1 13.8 .2 .3 .2 .1 S.D. .48 .2 .3 .3 .3 .3		z	•		<u> </u>		Ξ	17:7 111			. =		12.	7: ⊆
67KG 5.0. .68 1.06 3.41 2.28 .1 .0 .2 N 18 10 10 10 11 11 18 67KG 5.0. .27 13.0 10.7 .2 .1 .2 67KG 5.0. .2 .2 .2 .1 .2 67KG 5.0. .2 .2 .1 .1 .2 10 10 10 .1 .16 .1 10 10 .2 .1 .1 10 10 .2 .1 10 .2 .2 .2 5.0. .48 .2.48 .3	F .	MEGN		1.8	1.6		12.2			•	•) (•
N	00 MGZKG.	. O.S.		.68	1.06		4.4	表 2		4.	은 구 -		N o	. .
HEAN 1.1 13.8 .3 .2 .1 .2 .1 .2 .2 .1 .2 .1 .2 .1 .18 .18 .19 .10 .2 .1 .18 .18 .18 .19 .10 .10 .10 .10 .10 .10 .10 .10 .10 .10		z		=	<u>=</u>		Ξ	Ξ.		=	Ξ.		: =	
NAME	4 00	E d		1.5	2.7		13.0	10.7		. 7	+		C	c
MEAN 1.1 13.8 .3 .2 .2 .2 5.048 2.48 2.48	UU 1713/1415	⊃. z		ર્દ. ±	1.7J·		2.81	5.38			: - :		. ≖ :	! -
MEAN 1.1 13.8 .3 S.B48 2.48	١			: !	: -		:	=		=	Ξ,		≠ -	Ξ
	. I RE	mean o.o.	1.1 .48			13.8 2.48			nj S			.5		

TABLE 6 - CONTRIBUTORS NEBRINGO GALUES SUBMENUL FOXICITY STUDY IN ROLS

* * 	9 . 3. 4.	0.	.0.1 10			. 0. . 666 10	0. 0. 0. 0. 0. 0. 0. 0. 0. 0. 0. 0. 0. 0.	o. # =	0. ##	
Sn 1H70L030 - MH8 5	6 .00 0.00 0.00	. 00 10	6 . 00.	. 00 . 01		e	0.	o . 8. 4	0. 2. 2. 2. 2. 2. 2. 2. 2. 2. 2. 2. 2. 2.	
BASII *					0 .00.0					
	riEAN S.D.	MEAN S.D. N	MEAN S.D. N	MEAN 5.0.	MEAN S.D. N	MEAN S.D.	МЕРN S.D.	MEAN S.D.	MEAN S.D. v	MEAN 8.D.
GROUP AND DOSAGE LEVEL	1 0 MS/KG	2 100 MG/KG	3 200 MSZKG	4 800 MS/KG	5 RASELINE	1 0 MG/KR	2 186 MSZKG	3 200 MSZKB	4 800 MS/KG	5 BASELINE

FFMALF

THEM LETHERM CHEMISTRY ORIGINS SUBCHRUND TRACETY STUDY IN RATS

1 NEAN 0 NISZKÉ S.D. N 2 NEAN 100 MISZKÉ S.D. N 3 NEAN 8110 MISZKÉ S.D. N 4 NEAN 8110 MISZKÉ S.D. N 1 NEAN 0 MISZKÉ S.D. N	#				* ' ' ' ' ' '		: : : : : : : : : : : : : : : : : : :	24 17				
7, 7, 7, 7, 7, 7, 7, 7, 7, 7, 7, 7, 7, 7			13	*		¥	1	9	, , , , , , , , , , , , , , , , , , ,	-1-		: : : :
3,7 KG 3,7 KG 7,7 KG						in the second se	l		†	; ; ; ; ;	1 · · · · · · · · · · · · · · · · · · ·	1
7. KG	₹ ∴	148.0 1.56	146.1		6.01	6.25 F		104.5 3.21	104.3 2.00		6.0 ¥	6.3
3./kG ./kG		3	=		=	=		-	E.		<u> </u>	2
, KG	3 c	146.7 1 34	146.0		6.31	6.30		104.6	103.7		6.1	6.9
, kG		10	10		107: 10	9HZ.		2.74 16	1.75 113		.20	1 <u>2</u>
, KG , KG	7	147.3	145.5		6.37	6.18		104.0	104 4		u	
, kG		1.50	1.65		.333	3:5		2.15	3.12		. 2.0	.12
, kG		•	3		=	=		=	=		==	0 1
5 × 5	¥ .	147.6	146.0		6.56 s	6.58		105.0	104.7		5.9	6.5
, ×6	•	10.	10		955. 1	\$ =		2.79 10	2.52 Ju		. 15 0.0	n::
	7			6.61			103.4			u	} -	•
	2.13			.296			<u>.</u>			₹ w		
	•					a word .	а 14					
	Z.	145.3	144.5		5.71	6.16		106.0	106.0		6.1	6.7
2		B7 : 7	1.29 10			, 38. E		80 C	1.71		4	. 7° €
	z	144.0	145					:			=	=
100 MG/KG S.D.		96 . -	147.0		٠. ٠ ٢. ٠	6.14		106.4	106.8		6.1	6.7
z		9-	=======================================		18. 18.	2 E		7.3 H	= 		i =	4.5
	z	145.2	144.4		6.13 s	5.98		107.2	106.3		6	7
2 80 1157 KG 5.D. N		5. <u>=</u>	1.23		્રે કું •	(* ∓ *T =		47 20 54	2.23		i Š	
)	;		7	=		=	=		Ξ	9.
800 1137KG S.D.	z .	145.4 1.56	144.6		6.16 s	6.22		105.3	106.2		6.2	6.8
z •		0.1			: :=	# # !		20 7. 2 7.	-, -, -, -,		÷ <u>=</u>	- =
5 MEAN BriseLine S.D.	145.5 1.57			6.52			106.7			9.6		
										; ; ;		

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TARLE 7 - CURTINED IFRALCLINIER ORLUES SUBCHRÜLE TUSTELT STUDY IN RATS

Fight State Stat	Fight Figh	DUSAGE	*	* 11 F.F.	MEEE	13	-1	() () () () ()	* 1 ** - 1	1		1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1		un.	*** 1 *** 1
No.	FIGH 1.60 1.45 1.60 1.60 1.60 1.60 1.60 1.60 1.60 1.60 1.60 1.60 1.60 1.60 1.60 1.60 1.60 1.60 1.60 1.60 1.60 1.60 1.60 1.60 1.60 1.60 1.60 1.60 1.60 1.60 1.60 1.60 1.60 1.60 1.60 1.60 1.60 1.60 1.60 1.60 1.60 1.60 1.60 1.60 1.60 1.60 1.60 1.60 1.60 1.60 1.60 1.60 1.60 1.60 1.60 1.60 1.60 1.60 1.60 1.60 1.60 1.60 1.60 1.60 1.60 1.60 1.60 1.60 1.60 1.60 1.60 1.60 1.60 1.60 1.60 1.60 1.60 1.60 1.60 1.60 1.60 1.60 1.60 1.60 1.60 1.60 1.60 1.60 1.60 1.60 1.60 <th< th=""><th>!</th><th>*</th><th> </th><th>1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1</th><th>1</th><th>! ! !</th><th></th><th>* @Z</th><th>1 14</th><th>: ! !</th><th>F I I I I</th><th>t 1 1 1 - 3 1</th><th></th><th></th></th<>	!	*	 	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	1	! ! !		* @Z	1 14	: ! !	F I I I I	t 1 1 1 - 3 1		
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TABLE 7 - CONTINUED MEAN CLINIÇAL CHEMISTRY VALUES SUBCHRUNIC-TOXICITY STUDY IN RAFS

1		T - *	6	* *	7	vo	13	-1-	us	13	-1	9	13
1		•					MALE	щ					
U MIS/KIS	HEAN S.D. N		81 F 18.6 9 a	63 9.5 10		27 5.8 9.8	24 A 3.7		140 F 44.1 10	74 28.2 18		365 192.5 9.8	215 123.0
2 100 MG/KG	MEAN S.D.		72 7.6 10	5.8 9.9 10		24 2.9 10	21 4.1		117 17.0 10	80 14.4 10		466 214.4	251 162.1
3 200 MG/KG	MEAN S.D.		4 , 01, 10	67 28.4 18		26 4.9 10	26 9.5 16		136 35.7 10	69 15.7		352 192.4	268 153.3
4 800 MG/KG	MERN S.D.		79 20.4 10	66 15.1 10		28 5.5 10	33 \$ 8.8		105 19.2	23.7		374 209.1	220 138.4
5 BASELINE	MEAN S.D. N	96 56.7			28 7.8 5			201 56.7 5			372 255.8	2	2
							FEMALE	LE LE					
1 0 MG/KG	MEAN S.D.		79 16.3 10	73 13.1 10		25 3.9 10	22 5.5 10		101 26.3 18	47 8.8 10		402 187.3	311 A 155.2
2 100 MG/KG	MERN S.D.		82 13.6 10	71 14.9 10		28 7.3 10	25 6.1 10		100 44.8 10	58 21.1 10		382 119.2 10	261 136.4
3 200 MG/KG	MEAN S.D.		77 10.1 10	66 7.1 18		. 24 3.5	24 3.8 10		94 15.7 10	54 13.2 10		442 179.3 10	223 22.6 10
800 MG/KG	MEAN S.D.		K 8.9	65 13.2 10		25 4.3 10	29 9.1		82 25.4 10	49 18.8		391 209.6 10	260 136.2 10
BASELINE	MEAN S.D. N	102 20.2 5			3.7			165 33.2 5			580 91.3 5		

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a One animal deleted from statistics; see individual data (Appendix 7).

THEAN DUTHITHE CHEMISTRY UNLUES SHIEGHRINGE TOXICHTY STUDY IN RATS

GROUP AND		3 B	MSZDI		CREAL	EL - 111 - 121	-	+51.010.159	154 GR-49	*		HB (18,70)	1
DOSAGE	·	- ! !! !! !! !! !! !! !! !! !! !! !! !! !		13			\$1		1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	*	1-1	LIPS .	*
							MALE	벨					
1 0 MG∕KG	MERN S.D.		13 2.7 10	13 2.8 10		.7 91.9	. 3. 3.		8.5 8.5	103 11.0 11		62 12.0	84 F 20.5 10
2 100 MS/KG	MEAN S.D.		13 2.3 10	12 1.6 10		9. 0.1	. 5		89 5.5 18	109 6.9 10		56 14.7 10	76 24.9 10
3 200 MS∕KG	MEAN S.D. H		13 2.0 10	1.7 1.7 18		90. 11	. 5 3 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5		92 12.9 10	102 12.7 19		9.8 10	76 10.6 10
4 800 MG/KG	MEGN S.D.		14 5.3	13 4.2 10		. 9. 0. 0. 0. 0. 0. 0. 0. 0. 0. 0. 0. 0. 0.	9		989 8.1 10	100 14.0 18		6. 9. 9. 8.	47 13.8
5 нөseline	MEAN S.D. N	15 4.7 5			7 8 6			92 20.6 5			86 8.1.2 2.1.2		
							FP MAILE	FAI. E					
1 (i MS/KG	MEAN S.D.		16 2.9 10	1.9 1.9		7. 80. 01			90 7 90 1	95 F	•	26 14.7	93 18.3
2 10# MS/KG	MEAN S.D.		16 3.2 10	14 1.4 10		Ç ∂.≘	9 = =		91 7.0 9.0	88 ~ = 1		74 13.4	98 22.4 110
3 200 HS/KG	S.D.		13 4.1	13 2.0 10		Z = E	• = =		89 1.1.1 1.11	25. 4 10		83 15.5 18	20.5 20.5 10
4 8u0 MS/KG	MEAN S.D. M		4 % = 8	4. 4.01		9 . 11.	9 = =		89 4. ±	79 11. 5		95 8 14.3 11	133 S
5 1985ELINE	#EAN S.D.	15 2.2 2.3			> = ~			99 برع			68 7 4		

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THERM LETHICAL CHELLS IRV UNLIES SUBCHEUNT. 1821011Y STUDY IN RAIS

	# N	2011 25 1137 - 144 F.K	Q. *	1 8 1	11 1937fa METR	
		-1 5	13	;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;	13 ************************************	. ********
MEAN S.D.		8.9 1.02	8.64 8.64 8.64		.1 F	.2 .U6
_		10	10		3	01
MEAN		8.8	9.2		0	٠,
	·.	10	1.25) e	90.
EAN		6.8	8.1		₽.	.2
		.82	1.36	-	. U5	88.
		ļ	•		,	•
¥ Œ		9.1	7.		s 0·	2.
. z		69.	07.T	 O.
EAN	11.8			٦.		
S.D.	1.21			. UB.		
						FEMPLE
EAN		9.1	7.4 F		7.	.2
ა. ი. გ		$\frac{1.23}{10}$	$\frac{1.95}{10}$		8a. =	, U. 1.0
EAN		2.9	7.1		c	c
0		1.09	, v		• <u>`</u>	• = ·
z		10	0.1		D.	0.
EAN		9.4	7.3		.1	.2
oʻz		33. ±1	.8.5 10		÷ =	≆ <u>=</u>
MEAN		8.5 5.5	7.8		.	6 .
; : _		0.01	7 = 1		<u>=</u> =	: - - -
MEAN S.D.	12.0 1.21			- =		
	S			, us		

TABLE 8

*** PATH/IDX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 22-APR-88 PAGE: 53

STUDY NUMBER: 2399108

ABSOLUTE ORGAN WEIGHT MEANS (4)

TABLE INCLUDES: SEX-ALL;GROUP-ALL;WEEKS-ALL DEATH-T;SUBSET-ALL

 1 1 1 1	16	16 243.75 19.4	668 . 008	, 111 . 011	1.97	, 77 , 08	6. . 04
7	15	15 255.6 14.6	6 .070 .012	6 . 124 . 013	6 1.90 .06	6 .81 .06	6 .55
<u> </u>	20 19	9) <<< 20 258.4 14.8	10 .068 .009	18 . 115 . 019	10 1.93 .09	10 . 85 . 05	10 .54 .11
	20	4AL BODY WEIGHT (g) <<< 18 20 20 20 20 20 263.1 258.4 1.5 18.5 14.8	, , , , , , , , , , , , , , , , , , ,	< <p>15 .124 .029</p>	I/STEM <<< 15 1.97 .09	. 15 . 85 . 10	,,, 15 .54 .06
	18	TERMINAL BOD 18 437.0 ⁵ 61.5	>>> AD - ADRENAL <<< 5 B 15 .056 .051 .0 .013 .007 .0	- OVARY (()>> BR - BRAIN W/STEM <<< 5 8 15 :.09 2.01 1.97 .15 .11 .09	HEART <<<	SPLEEN . 67 .12
L	LE 3 15	>>> TE 15 472.5 30.8	, , , AD 5 . 056 . 013	- AO	2.09	,>> HT 5 1.25 .09	5 59
	2 17 1	17 478.6 74.7	7 .050	1 1 1 1 1 1 1 1	2.09	1.32	, 26 90.
	20	20 507.2 44.9	15 F .055	0	15 2.05 . 08	15 1.36 1.35	15 . 84 . 18
	SEX: GROUP: NUMBER:	# IN GRP.: M E A N : STAND DEU:	# IN GRP.: M E A N : STAND DEU:	# IN GRP.: M E A N : STAND DEU:	# IN GRP.: M E A N : STAND DEU:	# IN GRP.: N E A N : STAND DEU:	# IN GRP.: # E A N : STAND DEU:

*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

ABSOLUTE ORGAN WEIGHT MEANS (9)

PRINTED: 22-APR-88 PAGE: 54

STUDY NUMBER: 2399108

TABLE INCLUDES: SEX-ALL;GROUP-ALL;WEEKS-ALL DEATH-T;SUBSET-ALL

				. 1
	16	6 1.91 .13	6, 7,89 7,99	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
4	20 15 16	6 1.87	6 7.81 1.71	. •
i i	20	10 1.84 .20	10 7.78 1.21	0
1	20	, 16	; 15 7.39 1.49	TESTIS/EPIDID <<<
1	18	. KIDNEY <<< 8 3.21	- LIUER <<< 8 12.51 1.44	1
[F	15	>>> KD 5 3.27 3.27	>>> LI - 5 12.79 1.66	>>> TP 5 5.15 .21
MAI E	17	7 3.03 .29	7 12.72 1.20	5.07 5.44
!	20	15 3.22 .31	15 13.11 1.83	15 5.16 .35
SEX:		# IN GRP.: M E. A N : STAND DEU:	# IN GRP.: M E A N : STAND DEU:	# IN GRP.: M E A N : STAND DEU:

*** PATH/TOX SYSTEM OUTPUT *** SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 22-APR-88 PAGE: 55

STUDY NUMBER: 2399108

ORGAN TO TERMINAL BODY WEIGHT RATIO MEANS (%)

TABLE INCLUDES: SEX*ALL;GROUP*ALL;WEEKS*ALL DEATH*T;SUBSET*ALL

			-			
16	6 .0280 .0035	6 .0458 .0854	د 1815 1873ء	6 .318 .017	6 .219 .011	6 . 789 . 051
LE	6 .0286 .0047	6 . 0505 . 0038	6 .775 .047	6 .332 .025	6 . 225 . 041	6 .762 .055
FEMALE3 2 15	10 .0264 .0045	10 .0444 .0056	10 .750 .064	10 .327 .023	10 .207 .033	10 .713 .088
20	. 0258 . 0050	, 15 0 .0477 .0123	STEM <<< 15	, 15 f , 323	, 15 15 , 204 , 027	, 073
18	>>> AD - ADRENAL 5 8 8 .0114 .0128	- 0VARY < < <	5) BR - BRAIN W/STEM << 5 8 8 15 6427 .469 .754 .036 .038 .063	- HEART << 8 .262 .031	- SPLEEN <	- KIDNEY << 8 . 749 S . 046
E 3	>>> AD 5 .0114	- no < <	,> BR 5 .427 .036	>>> HT 5 .256 .024	>>> SP - 5 5 .161 .027	>>> KD 5 .666 .024
	. 0119 . 0046	0	7 .496 .184	, 312 , 112	, 180 . 067	7 .732 .339
20	15 . 0110 . 0019	0	15 F .404 .039	15 F .266	15 .164 .034	15 .630 .047
SEX: GROUP: NUMBER:	# IN GRP.: M E A N : STAND DEV:	# IN GRP.: M E A N : STAND DEU:	# IN GRP.: M E A N : STAND DEV:	# IN GRP.: M E A N : STAND DEU:	# IN GRP.: M E A N : STAND DEV:	# IN GRP.: M E A N : STAND DEU:

TABLE 9 *** PATH/TOX SYSTEM OUTPUT *** SUBCHRONIC TOXICITY STUDY IN RATS

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THUE: 70

STUDY NUMBER: 2399108

ORGAN TO TERMINAL BODY WEIGHT RATIO MEANS (%)

TABLE INCLUDES: SEX*ALL;GROUP-ALL;WEEKS*ALL DEATH=T;SUBSET*ALL

1 1 1 1	16	***************************************	3.266	.373		0	
	15	· · · · · · · · · · · · · · · · · · ·	3,195	.712	: 	0	
FEMA	20 15	9	3.022			0	
1	2.0			.569	>>> TP - TESTIS/EPIDID <<<	0	
1 1 1 1 1 1		>>> L1 - LIUER <<<	2.908	.253	- TEST15/E	8 1.171	100
	15	,,, []	2.604	.239		5 1,055	1000
Jen		,	3.037	1.266	; ; ; ; ; ; ;	7 1.203	777
1 1 1 1 1 1 1 1	20		2.567 A 3.037	.312	 	15 1.014	200
SEX	GROUP: NUMBER:	# [N GRP.: 15	MEAN	STAND DEV:	# # < # #	# IN GRP.:	CIANO DELL

TABLE 10A *** PATH/TOX SYSTEM OUTPUT *** SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 22-APR-88 PAGE: 57

GROSS	GROSS PATHOLOGY INCIDENCE	ICE SU	SUMMARY	1	1		1		STUDY NUMBER: 2399108
		2	N S	8 73 52	0 -	Œ 1	z z	M A L	S-AFFECTED
TABLE INCLUDES: SEX=ALL;GROUP=ALL;WEEKS=ALL	SEX:	1 1 1	MALE-		-	! ! !	-FEMALE-	1	-
DEATH=T;SUBSET=ALL	GROUP:	-1-	-2-	-3-	4	-1-	-2-	-3-	-4-
ORGAN AND KEYWORD(S) OR PHRASE	NUMBER	20	17	15	18	20	20 .	15	16
** TOP OF LIST ** BRAIN W/STEM (BR)	NUMBER EXAMINED: NOT REMARKABLE:		17	15	18 18	20	20	15	16 16
PITUITARY (PI)	NUMBER EXAMINED: NOT REMARKABLE:	20 20	17	15 15	18 18	20 20	20 20	15	16 16
CORD, CERUICAL (CS)	NUMBER EXAMINED: NOT REMARKABLE:	20 20	17	15	18 18	20 20	20	15	16 16
CORD, THORACIC (TC)	NUMBER EXAMINED: NOT REMARKABLE:	20 20	17	15 15	18 18	20 20	20 20	15 15	16 16
CORD, LUMBAR (LC)	NUMBER EXAMINED: NOT REMARKABLE:	20	17	15	18 18	20 20	20	15	16 16
NERUE, SCIATIC (SN)	NUMBER EXAMINED: NOT REMARKABLE:	20	17	15	18 18	20	20 20	15 15	16 16
LUNG (LU)	NUMBER EXAMINED: NOT REMARKABLE:	20 20	17	15 15	18 17	20	20 20	15	16 16
DARK AREA		0	•	•		0	0	0	0

TABLE 10A *** PATH/TOX SYSTEM OUTPUT *** SUBCHRONIC TOXICITY STUDY IN RATS

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# 1 1 1 1 1 1 1 1 1			

GROSS	PATHOLOGY INCIDENCE		SUMMARY	! !	; ; ;	1	1	us	STUDY NUMBER: 2399108
TABLE LINES		Z :	<u>ت</u> ت	8 E R	0 -	A	Σ 	A L S	- AFFECTED
SEX=ALL;GROUP=ALL;WEEKS=ALL DEATH-I;SUBSET=ALL	SEX:	1	MALE	1	-	1	-FEMALE-	1	1
	GROUP:	-1-	-2-	1	4	-1-	-23-	-4-	
ORGAN AND KEYWORD(S) OR PHRASE	NUMBER	20	12	15	18	20	20 15	15 16	
KIDNEY (KD)	NUMBER EXAMINED: NOT REMARKABLE:	20	17	15	18 16	20 18			16 16
PELVIS, DILATED PELVIS, FLUID PELVIS, GRANULAR MATERIAL PALE AREA H-PELVIS, DILATED		10001	00000	-0000	00117		. 00000	00000	
ADRENAL, MEDULLA (AM)	NUMBER EXAMINED: NOT REMARKABLE:	20 20	17	15	18 18	20	20 1 20 1	15 16 15 16	10.10
ADRENAL, CORTEX (AC)	NUMBER EXAMINED: NOT REMARKABLE;	20 20	17	15 15	18 18	20	20 1 20 1	15 16 15 16	
LIVER (LI)	NUMBER EXAMINED: NOT REMARKABLE:	20	17	15 15	18 17	20	20 1 20 1	15 16 15 16	
RAISED AREA		0	0	0		0	0	0	0
SPLEEN (SP)	NUMBER EXAMINED: NOT REMARKABLE:	20	17	15 15	18	20	20 1 20 1	15 16 15 16	
PANCREAS (PA)	NUMBER EXAMINED: NOT REMARKABLE:	20 20	17	15 15	18	20 2	20 1 20 1	15 16 15 16	
HEART (HT)	NUMBER EXAMINED: NOT REMARKABLE:	20 20	17	15 15	18 18	20 2	20 15 20 15	5 16 5 16	

TABLE 10A *** PATH/TDX SYSTEM OUTPUT *** SUBCHRONIC TOXICITY STUDY IN RATS

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STUDY NUMBER: 2399108 ۵ ليا -J ш <u>ن</u>ا نا Œ 1 16 1,19 16 16 16 16 16 16 16 16 16 16 16 4------FEMALE----Ų) نـ Œ -3-15 15 15 15 15 15 15 15 15 15 15 15 Ξ – z $\frac{20}{20}$ 20 20 20 20 2020 20 20 20 20 20 2020 20 -2-Œ 1 4 28 20 20 20 20 20 20 20 20 20 20 20 20 20 0 ш 0 18 18 19 18 18 18 18 18 18 18 18 18 18 18 18 18 0 -4----MALE----1 œ ш -3-15 15 15 0 15 15 15 15 15 15 15 15 12 • GROSS PATHOLOGY INCIDENCE SUMMARY E ⊐ Z 17 17 17 17 17 17 17 17 0 17 -2-20 20 0 -1-20 20 20 20 20 20 20 20 20 20 20 SEX: GROUP: NUMBER EXAMINED: NOT REMARKABLE: NUMBER EXAMINED: NOT REMARKABLE: NUMBER EXAMINED: NOT REMARKABLE: NUMBER EXAMINED: NUMBER EXAMINED: NOT REMARKABLE: NUMBER EXAMINED: NOT REMARKABLE: NUMBER EXAMINED: NOT REMARKABLE: NUMBER EXAMINED: NOT REMARKABLE: NUMBER: SEX=ALL;GROUP=ALL;WEEKS=ALL DEATH=T;SUBSET=ALL ORGAN AND KEYWORD(S) OR PHRASE (98) 9 PARATHYROID (PT) (ST) 녆 (ES) AORTA, THORACIC TABLE INCLUDES: (TR) 3 MAND SALIVARY (HE) DARK AREA **STOMACH, GL ESOPHAGUS** THYR01D TRACHEA THYMUS

TABLE 10A *** PATH/TOX SYSTEM QUTPUT *** SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 22-APR-88 PAGE: 60

GROSS PATHOLOGY INCIDENCE SUMMARY

STUDY NUMBER: 2399108

		Z -	E D	9 5 8	0 -	F - A	z	₩ E	S-AFFECT	E D
TABLE INCLUDES: SEX-ALL;GROUP-ALL;WEEKS-ALL	SEX	1	MALE	77 	į	. !	FEMALE-	<u> </u>	1 :	
DEATH-T;SUBSET-ALL	GROUP:	-1-	-2-	<u>-</u> ,	4-	-1-	-2	Ę-	-4-	
ORGAN AND KEYWORD(S) OR PHRASE	NUMBER:	20	17	15	18	20	20	15	16	
STOMACH, NOWGL (SU)	NUMBER EXAMINED: NOT REMARKABLE:	20	17	15	18 18	20 20	20 20	15 15	16 15	
WALL, THICKENED RAISED AREA			00	0 0	00	0	00	00		
DUGDENUM (DU)	NUMBER EXAMINED: NOT REMARKABLE:	20 20	17	15 15	18 18	20 28	20 20	15	16 16	
JEJUNUM (JE)	NUMBER EXAMINED: NOT REMARKABLE:	20 20	17	15 15	18	20 20	20	15	16 16	
ILEUM (1L) NUI	NUMBER EXAMINED: NOT REMARKABLE:	20	17	15 15	18 18	20 20	20 20	15	16 16	
CECLM (CE)	NUMBER EXAMINED: NOT REMARKABLE:	20	17	15 15	18 18	20 19	20	15	16 15	•
DARK AREA		0	•	0	0	-	0	0		
COLON (CD)	NUMBER EXAMINED: NOT REMARKABLE:	20 20	17	15	18 18	20 20	20	15 15	16 16	
RECTUM (RE) NUI	NUMBER EXAMINED: NOT REMARKABLE:	20 20	17	15 15	18 18	20 20	20 20	15 15	16 16	

TABLE 10A *** PATH/TOX SYSTEM OUTPUT *** SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 22-APR-88 PAGE: 61

GROSS	GROSS PATHOLOGY INCIDENCE		SUMMARY					STUDY NUMBER: 2399108
		z	B H D	E E	- 0 -	. Z	4 H	LS-AFFECTED
TABLE INCLUDES: SEX=ALL;GROUP=ALL;WEEKS=ALL	SEX: -		-MALE	 	 	FE	FEMALE	:
DEATH+T;SUBSET+ALL	GROUP:	-1-	-2:	.	-41-	-2-	Ę,	-4-
ORGAN AND KEYWORD(S) OR PHRASE	NUMBER:	20	4	15	10 26	26 20	15	16
LN, MESENTERIC (MS)	NUMBER EXAMINED: NOT REMARKABLE:	20	17	15	18 2 18 2	28 20 20 20	15 15	16 15
DARK AREA		•	0	0	0	0 0	0	
TESTIS (TE)	NUMBER EXAMINED: NOT REMARKABLE:	20	17	15	18 18	00	00	00
SOFT PALE CYST		000		0 0 0	000	000	000	0 0 0
EPIDIDYMIS (EP)	NUMBER EXAMINED: NOT REMARKABLE:	20	17	15	18 18	00	00	0 0
DUARY (DU)	NUMBER EXAMINED: NOT REMARKABLE:	00	0 0	00	00	20 20 20 20	15	16 16
UTERUS (UT)	NUMBER EXAMINED: NOT REMARKABLE:	00	0.0		0 0	20 20 17 19	15	16 14
LUMEN, FLUID		0	0	0	0	3 1	2	2
URINARY BLADDER (UB)	HUMBER EXAMINED: NOT REMARKABLE:	20 20	17	15 1	18 2 18 2	20 20 20 20	15	16 16

TABLE 10A *** PATH/TOX SYSTEM OUTPUT *** SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 22-APR-89 PAGE: 62

GROSS PATHOLOGY INCIDENCE SUMMARY

STUDY NUMBER: 2399108 0 F u W AFF 4 16 -----FEMALE-----16 16 16 16 16 16 16 16 16 16 ហ Φ -3-15 0 0 15 15 12 15 15 15 15 Σ -2-20 00 20 20 19 20 20 20 20 20 20 z σ 20 20 -1-00 20 20 20 20 20 20 20 19 ш 0 4-------HALE-----18 18 18 19 18 18 18 18 18 18 18 18 œ ш -3-15 15 15 15 15 15 15 15 15 15 15 0 E I Z -2-17 17 17 17 17 17 17 17 20 -1-20 20 20 20 20 20 20 20 20 20 SEX: GROUP: NUMBER: NUMBER EXANINED: MAMMARY GLAND (MG) NUMBER EXAMINED: (SM) NUMBER EXAMINED: NOT REMARKABLE: NUMBER EXAMINED: NOT REMARKABLE: NOT REMARKABLE: NUMBER EXAMINED: NOT REMARKABLE: SEX=ALL;GROUP=ALL;WEEKS=ALL DEATH=T;SUBSET=ALL DRGAN AND KEYWORD(S) OR PHRASE GLOBE RUPTURED POST MORTEM LACRIMAL GL, EXO (ED) MUSCLE, SKELETAL TABLE INCLUDES: (PR) DARK AREA MASS-UFL SKIN (SK) (EX) PROSTATE EYE

TABLE 19A *** PATH/TOX SYSTEM OUTPUT *** SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 22-APR-88 PAGE: 63

GROSS	GROSS PATHOLOGY INCIDENCE		SUMMARY		1	i ! !	 	; ; ;	STUDY NUMBER: 2399108
		!!	E S	8 E	0 -	ı L	Z Œ	A F	S-AFFECTED-
IABLE INCLUDES: SEX-ALL;GROUP-ALL;WEEKS-ALL	SEX:	1	MALE	, E	ł !	i !	FEMALE	HE.	! !
DEATH* ;SUBSE {**ALL	GROUP:	-1-	-2-	F	-4-	-1-	-2-	-3-	-4
ORGAN AND KEYWORD(S) OR PHRASE	NUMBER:	20	17	15	18	20	20	15	16
BONE, STERNUM (SB)	NUMBER EXAMINED: NOT REMARKABLE:	20	17	15	18 18	20	20	15 15	16 16
MARROW, STERNUM (SE)	NUMBER EXAMINED: NOT REMARKABLE:	20	17	15 15	18 18	20 20	20	15 15	16 16
BONE, FEMUR (FE)	NUMBER EXAMINED: NOT REMARKABLE:	28 20	17	15	18 18	20	20 20	15 15	16 16
SKIN, DTHER (SS)	NUMBER EXAMINED: NOT REMARKABLE:	20 20	17	15 15	18 18	2.0 2.0	20	15 15	16 16
LN, OTHER (LN)	NUMBER EXAMINED: NOT REMARKABLE:	20 20	17	15	18 18	. 20	2.0 2.0	15	16 16
^COLLECTED/TAKEN (XW)	NUMBER EXAMINED: NOT REMARKABLE:	20 15	17 2	15	18 8	20 15	20	15	16 6
ELECTRON MICROSCOPY SAMPLE ** END OF LIST **		3	10	18	10	ī.	10	•	10

TABLE 10B *** PATH/TOX SYSTEM DUTPUT *** SUBCHRONIC TOXIC1TY STUDY IN RATS

PRINTED: 22-APR-88 PAGE: 64

GROSS F	GROSS PATHOLOGY INCIDENCE SUMMARY	S SUM	MARY				8 8 1 1	STUDY NUMBER: 2399108	R: 2399108
	,	N N	O M B	ш Ж	1 F	Ζ Œ	E E	LS-AFFE	C T E D
TABLE INCLUDES: SEX-ALL;GROUP-ALL;WEEKS-ALL	SEX:		MALE	ļ	!	- 1	-FEMALE	 	
DEATH-UNSCHED;SUBSET-T	GROUP:	-1-	-2-	.3t-	-41-	-2-	-3-	-4-	
ORGAN AND KEYWORD(S) OR PHRASE	-			ic	5	60	· ·	4	
** TOP OF LIST ** BRAIN W/STEM (BR)	NUMBER EXAMINED:	' 00	, M-	rv.4.	. 88		, , , , , , , , , , , , , , , , , , , ,	44	
SOFT		0	5	1	0	0	•	0	
PITUITARY (PI)	NUMBER EXAMINED: NOT REMARKABLE:	0 9	m m	ro ro	2 2	00	rv rv	44	
CORD, CERUICAL (CS)	NUMBER EXANTMED: NOT REMARKABLE:	c o	mm	10 IO	0.01	00	rv rv	44	
CORD, THORACIC (TC)	NUMBER EXAMINED: NOT REMARKABLE:	0 0	M M	מימ	8.8		rv rv	4.4	
CORD, LUMBAR (LC)	NUMBER EXAMINED: NOT REMARKABLE:	o o	m m	R R	0.01	00	RR	44	
NERUE, SCIATIC (SN)	NUMBER EXAMINED: NOT REMARKABLE:	0 0	ww	rv rv	22	00	ייטייסי	44	
TUNG (LU)	NUMBER EXAMINED: NOT REMARKABLE:	00	r =	r o	0.0	0 0	n a	40	
FAILURE TO COLLAPSE MOTTLED		. .	0	æ æ	2.2	0 0	ינייני	44	

TABLE 10B *** PATH/TOX SYSTEM OUTPUT *** SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 22-APR-88 PAGE: 65

STUDY NUMBER: 2399108

GROSS PATHOLOGY INCIDENCE SUMMARY

CTED ---AFFE 44 44 4 44 141 4 ---FEMALE----G R R 10 IO ic ic Œ Ķ 6 6 Ŗ R R т - х - ч 00 00 00 0 00 00 00 -2-0 00 0 0 0 0 00 0 00 ----0 ш 0 2 0 20 20 20 2 0 20 -4ı œ -----HALE----5 8 50 5 --- NUMBE -3-S 5 50 m m m m -2-M M 00 00 00 --00 --0 0 0 0 1 NOT REMARKABLE: NUMBER EXAMINED: NUMBER EXAMINED:NUMBER EXAMINED:.....NUMBER EXAMINED:... NOT REMARKABLE: NUMBER EXAMINED: SEX LIVER (LI)NUMBER EXAMINED: GROUP: NUMBER EXAMINED: NOT REMARKABLE: NUMBER EXAMINED: NOT REMARKABLE: 1 1 1 1 1 1 1 1 NUMBER: SPLEEN (SP) ORGAN AND KEYWORD(S) OR PHRASE SEX=ALL;GROUP=ALL;WEEKS=ALL DEATH=UNSCHED;SUBSET=T ADRENAL, MEDULLA (AM) 9 ADRENAL, CORTEX (PA TABLE INCLUDES: H-ENLARGED Œ KIDNEY (KD) HEART (HT) PANCREAS THYMUS

TABLE 10B *** PATH/TOX SYSTEM OUTPUT *** SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 22-APR-88 PAGE: 66

GROSS	S PATHOLOGY INCIDENCE		SUMMARY	i 1 1	1 1 1 1				
TABLE INCLUDES:		z !	UMB	п Қ	L	Z C	A H I	LS-AFFECTED	
SEX=ALL;GROUP=ALL;WEEKS=ALL DEATH=UNSCHED;SUBSET=T	SEX:	MALE	-MALE			FEMALE	1AL.E		
	GROUP	-1-	-2-	-4- 	-41-	-2-	-3-	-4-	
ORGAN AND KEYWORD(S) OR PHRASE	NUMBER:	6	w				R	4	
TRACHEA (TR)	NUMBER EXAM! NOT REMARKA			ן הייני	2 0		1 WW	# 44	
THYROID (TY)	. NUMBER EXAMINED: NOT REMARKABLE:	00	mm	re re	2 0	00	RR	4 4	
PARATHYROID (PT)	. NUMBER EXAMINED: NOT REMARKABLE:	00	W W	n n	2 0	0.0	r. r.	4 4	
ESOPHAGUS (ES)	. NUMBER EXAMINED: NOT REMARKABLE:	00	mm	ro ro	2 0	0 c	r r	4.4	
MAND SALIVARY GL (SG)	. NUMBER EXAMINED: NOT REMARKABLE:	. •	m m	r r	22	00	מיש	44	
AORTA, THORACIC (AD)	NUMBER EXAMINED: NOT REMARKABLE:	0 0	ww	ĸκ	2 0	0	rv rv	ч ч	
STOMACH, GL (ST)	NUMBER EXAMINED: NOT REMARKABLE:	0 0	MM	ى ما	2 1 0	0 0	r	44	
PALE AREA		0	0	0	1 0	0	•	0	
STOMACH, NONGL (SU)	NUMBER EXAMINED: NOT REMARKABLE:	0 0	m m	ro ro	2 0 2 0	00	r r	4.4	

TABLE 10B *** PATH/TOX SYSTEM OUTPUT *** SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 22-APR-88 PAGE: 67

STUDY NUMBER: 2399108 0 AFFECTE ı 0 4 4 0 0 4 -4-G 0 A M I M A 13 5 6 **6 6** in in 00 'n -----FEMALE-0 00 0 00 00 00 -2-- -_ - -0 0 0 00 00 00 00 0 0 00 : _ 0 Ŀ ٥ 20 20 0 20 20 14-N 2 2 2 -----HALE----2 ic ic R 4 5 50 10 -3ů, R 10 **10** 10 50 50 NUMBE GROSS PATHOLOGY INCIDENCE SUMMARY 0 mm m m P P -2-0 0 0 00 00 90 o o - -00 00 -1-NOT REMARKABLE: NUMBER EXAMINED: NOT REMARKABLE: GROUP: NUMBER EXAMINED: NOT REMARKABLE:NUMBER EXAMINED: RECTUM (RE)NUMBER EXAMINED: NOT REMARKABLE: SEX NUMBER EXAMINED: NUMBER EXAMINED: NOT REMARKABLE: NUMBER EXAMINED: NOT REMARKABLE: NUMBER: NOT REMARKABLE: LN, MESENTERIC (MS) TABLE INCLUDES: SEX-ALL;GROUP+ALL;WEEKS-ALL DEATH-UNSCHED;SUBSET+T DRGAN AND KEYWORD(S) OR PHRASE UNEQUALLY SIZED DUCOENUM (DU) (JE) TESTIS (TE) (00) \exists (CE) JEJUNUM ILEUM CECUM COLON

TABLE 10B *** PATH/TOX SYSTEM OUTPUT *** SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 22-APR-88 PAGE: 68

GROSS	PATHOLOGY INCIDENCE		SUMMARY	!	i :	i I I I		STUDY NUMBER: 2399108
TABLE INCLINES:	'	Z 	U M B	ЕЛ СК 1	0 F	Z Z	A L	S-AFFECTED
SEX+ALL JGROUP-ALL JWEEKS-ALL DEATH-INSCHED: SIRSFT-T	SEX:	MALE	-MALE-	!		FEMALE-	ALE	
	GROUP:	-1-	-23-	-4-	-1-	-2-	F.	-4-
ORGAN AND KEYWORD(S) OR PHRASE	NUMBER:	0	۳.	א			ĸ	4
EPIDIDYMIS (EP)	NUMBER EXAMINED: NOT REMARKABLE:		mm		22		. 00	; 00
OUARY (DU)	NUMBER EXAMINED: NOT REMARKABLE:	0 0	00	0.0	0 0			
UTERUS (UT)	NUMBER EXAMINED: NOT REMARKABLE:	- -	00		0 0	.	r. r.	44
URINARY BLADDER (UB)	NUMBER EXAMINED: NOT REMARKABLE:	00	m m	וני וני	2 0	00	N IV	44
PROSTATE (PR)	NUMBER EXAMINED: NOT REMARKABLE;	00	₩ ₩	22	0.0	00	60	0
SEMINAL VESICLE (SU)	NUMBER EXAMINED: NOT REMARKABLE:	. 0	n m	2 2 2	0.0	0	00	0
SKIN (SK)	NUMBER EXAMINED: NOT REMARKABLE:	00	n n	5 2 2	0.0	00	n n	44
MAMMARY GLAND (MG)	NUMBER EXAMINED: NOT REMARKABLE:	00	mm	5.2	0 0	00	ææ	44

TABLE 10B *** PATH/TOX SYSTEM OUTPUT *** SUBCHRONIC TOXICITY STUDY IN RATS

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GROSS	GROSS PATHOLOGY INCIDENCE SUMMARY	E SUM	ARY			1	1	STUDY NUMBER: 2399108
		⊐ Z -	8	E R	- H O	Z Z	A L	S-AFFECTED
TABLE INCLUDES: SEX-ALL;GROUP-ALL;WEEKS-ALL	SEX1 -	 	-MALE-	! ! !		FEMALE-	LE	
DEATH-UNSCHED;SUBSET-T	GROUP: -	-12-	F	-4-	-1	-2-	-3-	-4-
ORGAN AND KEYWORD(S) OR PHRASE	NUMBER:	0	•	2	•	0 !	ن ما	4
MUSCLE, SKELETAL (SM)	NUMBER EXAMINED: NOT REMARKABLE:	00	W W	2 2 2	-	. .	re re	ধ্ব
EYE (EY)	NUMBER EXAMINED: NOT REMARKABLE:	0 0	n n	22	00		n n	44
LACRIMAL GL, EXO (EO)	NUMBER EXAMINED: NOT REMARKABLE:	00	nn	22	0 0	6	re re	4 W
DARK AREA		0	0	0		0	•	1
BONE, STERNUM (SB)	NUMBER EXAMINED: NOT REMARKABLE:	0	w w	22	. •	o o	т. г	44
MARROW, STERNUM (SE)	NUMBER EXAMINED: . NOT REMARKABLE:	0 0	nn	22	o o	00	n n	44
BONE, FEMUR (FE)	NUMBER EXAMINED: NOT REMARKABLE:	00	M M	22	0	0 0	n n	44
SKIN, OTHER (SS)	NUMBER EXAMINED: NOT REMARKABLE:	.	23	22		00	TL FL	44
SORE		•	-		0	•	0	0

TABLE 10B *** PATH/TOX ŞYSTEM OUTPUT *** SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 22-APR-88 PAGE: 70

GROSS PATHOLOGY INCIDENCE SUMMARY

STUDY NUMBER: 2399108

TABLE INCLIDES:		Z	Σ	9 E R	0 -	Œ I		AL	NUMBER - OF - ANIMALS - AFFECTED
SEX-ALL JGROUP-ALL JWEEKS-ALL	SEX	MALE	MAL	<u> </u>			FEMALE		
	GROUP: -12341234-	-1-	-2-	Ϋ́.	4-	-1-	22	¥.	-4-
ORGAN AND KEYWORD(S) OR PHRASE	NUMBER		۰ ا	ا ا ا	٠ ٢	0	ï • !	ا ا	4 1
LN, OTHER (LN)	. NUMBER EXAMINED:	0 =	m c	ıc u	60 6	.	0 0	rv n	4 4
ENLARGED ** END DF LIST **		• •	, ,		, 0	• •	• 0		t o

TABLE 11A *** PATH/TOX SYSTEM OUTPUT *** SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 22-APR-89 PAGE: 71

STUDY NUMBER: 2399108

HISTOPATHOLOGY INCIDENCE SUMMARY

٥ AFFECTE 16 16 16 16 16 16 15 16 16 16 16 16 16 -4-16 -----FEMALE-----ALS 00 -3-00 00 15 Z Z 00 00 00 0 = -2-20 00 20 20 20 20 $\frac{20}{20}$ 0 20 0 4 20 20 6 20 + 19 18 20 u 0 18 18 18 18 8 8 - -18 18 Œ -4-18 18 18 18 -----MALE---œ NUMBE **.** 0 - 0 0 -3 5 00 **-** -00 0 0 0 0 -2-00 ٥ م 20 20 20 20 0 20 20 20 1 1 2020 20 20 NOT REMARKABLE: NOT REMARKABLE: NUMBER EXAMINED: NOT REMARKABLE: SEX NUMBER EXAMINED: NOT REMARKABLE: NUMBER EXAMINED: NOT REMARKABLE: NUMBER EXAMINED: NOT REMARKABLE: GROUP: NUMBER: NOT REMARKABLE: CORD, LUMBAR (LC) SEX=ALL;GROUP=ALL;SCREEN=ALL;WEEKS=ALL DEATH=T;FIND=ALL;SUBSET=ALL CORD, THORACIC (TC) ORGAN AND FINDING DESCRIPTION -- UNILATERALLY EXAMINED EE. (AC) (<u>ś</u>) --VACUOL I ZATION --DEGENERATION BRAIN W/STEM (BR) ADRENAL, MEDULLA ** TOP OF LIST ** ADRENAL, CORTEX PITUITARY (PI) TABLE INCLUDES: CORD, CERVICAL --CYST

TABLE 11A *** PATH/TOX SYSTEM OUTPUT *** SUBCHRONIC TOXICITY STUDY IN RATS

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3TSTH	HISTOPATHOLOGY INCIDENCE SUMMARY	CE SUM	MARY	! ! !	1	!	. !	1 1 1	STUDY NUMBER: 2399108
TABLE INCLUDES:		Z !	E	8 R	0 -	٠ د	Σ Ξ	₩.	S-AFFECTED
SEX-ALL;GROUP-ALL;SCREEN-ALL;WEEKS-ALL DEATH-T;FIND-ALL;SUBSE;TALL	SEX:	; ; ;	MALE		· 	-	FEMALE	 	!
	GROUP:	-1-	-2-	-3-	-4-	+	-2	-3	4-
ORGAN AND FINDING DESCRIPTION	NUMBER:	20	17	15	18	20	20	15	16
TRACHEA (TR)	NUMBER EXAMINED: NOT REMARKABLE:	20		00			1		166
THYROID (TY)	NUMBER EXAMINED: NOT REMARKABLE:	20	6 0	00	18 18	20	00	= 0	16 16
PARATHYROID (PT)	NUMBER EXAMINED: NOT REMARKABLE:	12	0 0	0	12 12	12 12	0 C	0 0	15 15
ESOPHAGUS (ES)	NUMBER EXAMINED: NOT REMARKABLE:	20 20	0 8	- -	18 18	20	0 0	• •	16 16
LUNG (LU)	NUMBER EXAMINED: NOT REMARKABLE:	20	17	15	18 1	20	20 1 0	15	16 0
PERIBRONCHIAL/PERIVASCULAR, INFILTRATION, LYMPHOID FOREIGN MATERIAL PNEUMONITIS	۵	20 0 0	17 0 1	15 1	17 0 0	20 3 3	20 1 0	7 00	16 0 0
HEART (HT)	NUMBER EXAMINED: NOT REMARKABLE:	20 15	00	0 0	18 18	20 20	0 0		16 16
CARDIOMYOPATHY, DEGENERATIVE		īv	0	0	0	0	0	0	0
SPLEEN (SP)	NUMBER EXAMINED: NOT REMARKABLE:	20	0	c 0	18	20 20	0 0	0.0	16 16

TABLE 11A *** PATH/10X SYSTEM OUTPUT *** SUBCHRONIC TOXICITY STUDY IN RATS

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STUDY NUMBER: 2399108

HISTOPATHOLOGY INCIDENCE SUMMARY

HISTOPAT	HISTOPATHOLOGY INCIDENCE	E SUMMARY	ARY 	 	1	! ! !	1	" ¦	
		Z :	8 H D	m ox	- O F	Œ ;	Ξ	ALS	AFFECTED
TABLE INCLUDES:	SEX		MALE	1	\ 	FEMALE	EMALE	1	•
DEATH-TIFIND-ALL; SUBSET-ALL	GROUP:	-	-2	-3-	-4-	-12-	-5-		-4-
ORGAN AND FINDING DESCRIPTION	NUMBER:	20	12	15	18	20 2	20 15	1	16
LIVER (LI)	NUMBER EXAMINED: NOT REMARKABLE:	20 13	17	15 13	18 13	20 2	20 1 12 1	15 12	16 12
FOCT OF MONONUCLEAR CELLS		m •	mo	~ <		6 0 €	80 (5 0	40
FOCAL HEPATITIS BILE DUCT, INFLAMMATION, CHRONIC	,	- 10 C	- o c		. o r				0
(MULTI)FOCAL NECROSIS INJECTION SITE			-	0	-	0	0	0	0
	NUMBER EXAMINED: NOT REMARKABLE:	28 14	17 8	15	18 10	20	20 1	15 10	16 14
MEDIACTHY CHRONIC PROCRESSIVE		9	6.	6	~	n	4 0	R C	200
nernary Circuit Control Cont				∍ ~	o	, -	- m	. 0	. 6
PELVIS, DILATATION		0	0	 (→ •			= -	0 0
PyELON BITTIS			- -	0	- 0	90		, .	
	NUNBER EXAMINED: NOT REMARKABLE:	20 20	00	00	18 18	20 20	00	0	16 16
NO LISTENCE -		o	•	0	0	•	•		0
(ns)	NUMBER EXAMINED: NOT REMARKABLE:	20 20	00	00	18 18	20 20		00	16 15
ACANTHOSIS INFLAMMATION, CHRONIC		00	0 0	.	0 0	00	00	00	
	NUMBER EXAMINED: NOT REMARKABLE:	20 20	0 0	0	18 18	20 20		. .	16 16

TABLE 11A *** PATH/TOX SYSTEM OUTPUT *** SUBCHRONIC TOXICITY STUDY IN RATS

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STUDY NUMBER: 2399108 - AFFECTED 4-16 ----FEMALE----16 15 NIMALS 16 16 16 0 18 16 16 16 16 25 -3-15 00 -2-20 0 = 00 00 -20 20 20 20 19 20 $\frac{20}{20}$ 202 0 4 0 ------MALE-----4-18 18 19 88 18 18 18 18 0 œ -3 15 00 **-** -SUMMARY -2-1, 9 9 - -0 0 00 20 20 20 20 20 20 18 -20 20 0 20 20 20 0 HISTOPATHOLOGY INCIDENCE SEX GROUP: NUMBER: NUMBER EXAMINED: NUMBER EXAMINED: NOT REMARKABLE: NOT REMARKABLE: NUMBER EXAMINED: NUMBER EXAMINED: NOT REMARKABLE: NUMBER EXAMINED: NOT REMARKABLE: NOT REMARKABLE: (JE) SEX-ALL;GROUP-ALL;SCREEN-ALL;WEEKS-ALL DEATH-T;FIND-ALL;SUBSET-ALL ORGAN AND FINDING DESCRIPTION --INFLAMMATION, CHRONIC -- INJECTION SITE TABLE INCLUDES: -- CONGESTION PANCREAS (PA) RECTUM (RE) ILEUM (1L) CECUM (CE) 9 JEJUNUM COLON

TABLE 11A *** PATH/TOX SYSTEM GUTPUT *** SUBCHRONIC TOXICITY STUDY IN RAIS

PRINTED: 22-APR-88 PAGE: 75

STUDY NUMBER: 2399108 ٥ ш AFFECT 14-16 16 91 202 2 16 ຜ ANINAL -3-00 15 ----FEMALE 0 0 -2+ 20 00 ı -1-20 = 00 61 20 15 20 20 0 0 \Box Ŀ 0 -4-18 18 18 7 9 9 9 ------MAILE----ŧ œ --- NUMBE -3-15 HISTOPATHOLOGY INCIDENCE SUMMARY -2-0 17 20 20 20 - -20 00 -1-20 SEX GROUP: NUMBER: EPIDIDYMIS (EP) NUMBER EXAMINED: HOT REMARKABLE: NUMBER EXAMINED: NOT REMARKABLE: UTERUS (UT) NUMBER EXAMINED: NOT REMARKABLE: NUMBER EXAMINED: NUMBER EXAMINED: NOT REMARKABLE: TABLE INCLUDES: SEX-ALL;GROUP-ALL;SCREEN-ALL;WEEKS-ALL DEATH-T;FIND-ALL;SUBSET-ALL --INFLAMMATION, CHRONIC ACTIVE --MONONUCLEAR CELL INFILIRATE ORGAN AND FINDING DESCRIPTION -- UNILATERALLY EXAMINED --- MUCOSAL HYPERPLASIA PROSTATE (PR) URINARY BLADDER (UB) --DEGENERATION --DILATATION --CALCULUS TESTIS (TE) DUARY (DU)

TABLE 11A
*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RATS

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HISTO	HISTOPATHOLOGY INCIDENCE	HINS 30	SUMMARY		 				STUDY NUMBER: 2399108
TABLE INCLUDES:		z 	Σ	19 FF	- 0	F - A	Ξ - Z	1 A L	S-AFFECTED
SEX-ALL GROUP-ALL ; SCREEN-ALL ; WEEKS-ALL DEATH-T: FIND-ALL ; SIMSFT-ALL	SEX:	1	MALE-		-		FEMALE	Ē	1.
	GROUP:	1	-2-	# <u></u>	-4-	-1-	-2-	- 3 -	-4-
ORGAN AND FINDING DESCRIPTION	NUMBER:	20	12	15	138	100 -	20	15	16
SEMINAL VESICLE (SV)	NUMBER EXAMINED: NOT REMARKABLE:	20 20	0 0	00					00
INFLAMMATION, CHRONIC ACTIVE		0	c	0	-	•	0	0	0
SKIN (SK)	NUMBER EXAMINED: NOT REMARKABLE:	2.0 2.0	00	0 0	18	20 20	0 0	0 0	16 16
MAMMARY GLAND (MG)	NUMBER EXAMINED: NOT REMARKABLE:	18 18	60	90	13	20 20	10	0 0	14 14
M-ADENOCARCINOMA		•	٥	0	0	0		0	0
MUSCLE, SKELETAL (SM)	NUMBER EXAMINED: NOT REMARKABLE:	20	0 0	00	18	20 20	e ė		16 16
NERUE, SCIATIC (SN)	NUMBER EXAMINED: NOT REMARKABLE:	20 20	0 0	00	18 18	20	0 0	0 0	16 16
MAND SALIUARY GL (SG)	NUMBER EXAMÍNEO: NOT RENARKABLE:	20 20	00	• 0	18 18	20 20	0	00	16 16
THYMUS (TH)	NUMBER EXAMINED: NOT REMARKABLE:	19	0 0	0 0	18 18	20	00	00	16 16
AORTA, THORACIC (AO)	NUMBER EXAMINED: NOT REMARKABLE:	20 20	00	00	18 19	20 20	0 =	0	16 16

TABLE 11A *** PATH/TOX SYSTEM OUTPUT *** SUBCHRONIC TOXICITY STUDY IN RATS

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			,							
HISTO	HISTOPATHOLOGY INCIDENCE SUMMARY	SUS 3C	IMARY	1	1	1 1 1	; ; ;	 	STUDY NUMBER: 23	2399108
		1		- - -	R - 0	€ 1	z	MAL	S-AFFECTI	1
TABLE INCLUDES: SEX-ALL;GROUP-ALL;SCREEN-ALL;WEEKS-ALL	SEX:	1	MALE-	<u>.</u>			FEMALE-	I.E		
DEATH-T;FIND-ALL;SUBSET-ALL	GROUP:	+	-2-	Ķ	-4-	-	-2-	-3-	-4-	
ORGAN AND FINDING DESCRIPTION	NUMBER:	20	17	15	18	20	20	15	16	
EYE (EY)	NUMBER EXAMINED: NOT REMARKABLE:	20 13		0	18 17	20 18	00	0 0	16 13	
CHRONIC INFLAMMATION, HARDERIAN GLAND ONE EXAMINED		9 1	00	0	0	0 0	00	0	₩0	
LACRIMAL GL, EXD (EO)	NUMBER EXAMINED: NOT REMARKABLE:	20 17		0	18 18	20 20	00	00	16 16	
FOCAL MONONUCLEAR INFILTRATE		m	0	0	0	0	•	0	0	
BONE, STERNUM (SB)	NUMBER EXAMINED: NOT REMARKABLE:	20	00	0 0	18 18	20 20	0	0	16 16	
MARROW, STERNUM (SE)	NUMBER EXAMINED: NOT REMARKABLE:	20 20	00	0	18 17	20 20	00	90	16 16	
HYPERCELLULAR		0	0	ø		•	0	0	0	
BONE, FEMUR (FE)	NUMBER EXAMINED: NOT REMARKABLE:	20 19	o <u>e</u>	0	18 16	20 20	0	0 0	16 14	
ARTICULAR SURFACE NDT PRESENT		-	•	•	2	0	4	•	2	
LN, OTHER (LN)	NUMBER EXAMINED: NOT REMARKABLE:	e o	- -	0	0 0	00	. .	0	0.	
SKIN, OTHER (SS)	NUMBER EXAMINED: NOT REMARKABLE:	00	00	00	0 ¢	00	00	00	0 Đ	

** END OF LIST **

*** PATH/TOX SYSTEM DUTPUT *** SUBCHRONIC TOXICITY STUDY IN RATS

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HISTOPATHOLOGY INCIDENCE SUMMARY

STUDY NUMBER: 2399108 ۵ CTE AFFE , -4------FEM9LE-----4 S 4 - ANIMAL -3-S r r **10** 10 In In -2-00 00 90 00 00 0 -1-**-**00 00 80 - -<u>п</u> ------MALE-----N NO 20 20 20 20 20 œ NUMBE -3-S 5 S 10 io io E C E IS -2-MM mm ; ; -1-00 00 --9 @ 00 0 e 0 SEX GROUP: NUMBER: NUMBER EXAMINED: NOT REMARKABLE: NUMBER EXAMINED: NOT REMARKABLE: NUMBER EXAMINED: NOT REMARKABLE: NOT REMARKABLE: NUMBER EXAMINED: NOT REMARKABLE: NUMBER EXAMINED: NOT REMARKABLE: TABLE INCLUDES: SEX-ALL;GROUP-ALL;SCREEN-ALL;WEEKS-ALL DEATH-UNSCHED;FIND-ALL;SUBSET-ALL ORGAN AND FINDING DESCRIPTION --- UNILATERALLY EXAMINED -- UNILATERALLY EXAMINED ŝ (CS) (JE) TRACHEA (TR) ** TOP OF LIST ** BRAIN W/STEM (BR) (P) ADRENAL, CORTEX CORD, THORACIC CORD, CERVICAL PITUITARY

TABLE 11B *** PATH/TOX SYSTEM OUTPUT *** SUBCHRONIC TOXICITY STUDY IN RATS

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HISTOPATHOLOGY INCIDENCE SUMMARY	CIDENCE S	SUMMAR	_	1) 		STUDY NUMBER: 2399108	
		E II N	83 F3	R - 0 F	Œ	E - z	Ą	C T E D	
SEX-ALL; GROUP-ALL; SCREEN-ALL; WEEKS-ALL	SEXt	MALE	?E	!		FEMALE-			
UERIH-UNSCHED IF INVARLISUBSET-ALL	GROUP: -1-	-2-	-3-	4	-1-	-2-	-3-	-4-	
ORGAN AND FINDING DESCRIPTION	NUMBER: 0	n	1	8 1	œ ;	0 1	in, i	4 :	
THYROID (TY)	INED: 0 ABLE: 0	m m	44	88	00	90	6	44	
PARATHYROID (PT)	INED: 0	m m	M M	88	0 0	00	rv rv		
ESOPHAGUS (ES) NUMBER EXAMINED:	INED: 0	m m	w w	88	0 0	00	R R	4.4	
LUNG (LU)NUMBER EXAMINED:	INED: 0 ABLE: 0	K 1	r e	0.0	0 0	.	r 0	40	
PERIBRONCHIAL/PERIUASCULAR, INFILTRATION, LYMPHOIDFOREIGN BODY PNEUMONIACONGESTIONFOREIGN MATERIALFOREIGN MATERIAL	00000	00000	40-40	0	00000		rr-	2 4 0 0 2 2	
HEART (HT) NUMBER EXAMINED:	INED: 0	m m	r r	88	0	00	R, R	44	
SPLEEN (SP)	INED: 0	m m	s s	88	0 0	0 0	6 10	4.4	
LIVER (LI) NUMBER EXAMINED:	INED: 0	 w.c	N IV	00		0 0	r r	4.4	
FOCI OF MONONUCLEAR CELLS	0	-	0	0	0	0	0	0	

TABLE 11B *** PATH/TOX SYSTEM OUTPUT *** SUBCHRONIC TOXIC1TY STUDY IN RATS

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ID1S1H	HISTOPATHOLOGY INCIDENCE		SUMMARY						STUDY NUMBER:	1BER: 2399108	
		Z	E	9 5 8	0 -	F - F	A N I	H A L	SIA	FECTED	1 1
TABLE INCLUDES: SEX-ALL;GROUP-ALL;SCREEN-ALL;WEEKS-ALL	SEX:	!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!	MALE	E		FEMALE	-FEMA	LE	-		
DEATH-UNSCHED;FIND-ALL;SUBSET-ALL	GROUP:	-1-	-5-	Ļ	4-	-1-	-2-	Ę-	-4-		
ORGAN AND FINDING DESCRIPTION	NUMBER	0	M 1	6 1	2	۰	-	10.	4		*
KIDNEY (KD)	NUMBER EXAMINED: NOT REMARKABLE:	0	m m	r r	0.00	0 0	0	r. 4	44		
NEPHROPATHY, CHRONIC PROGRESSIVE PELVIS, DILATATION		0 0	- 0	• •	0 0	00	0 0		· • •		
STOMACH, GL (ST)	NUMBER EXAMINED: NOT REMARKABLE:	00	W W	44	22	0 C	0	r. r.	44		
STDMACH, NONGL (SU)	NUMBER EXAMINED: NOT REMARKABLE:	00	mm	N N	20		0 0	r. r.	44	 	
DUODENUM (DU)	NUMBER EXAMINED: NOT REMARKABLE:	0 0	2 2	m m	2 2	0 0	.0 0		m m		
JEJUNUM (JE)	NUMBER EXAMINED: NOT REMARKABLE:	0 0	2.2	mm	22	00	0 0	n n	W W		
וובטא (ונ)	NUMBER EXAMINED: NOT REMARKABLE:	00	0 0	2 2	0.00	00	00	r. r.	mm.		
PANCREAS (PA)	NUMBER EXAMINED: NOT REMARKABLE:	00	m m	v v	1	8 0	0 C	r, rc	44		
INFLAMMATION, CHRONIC		0	0	0	-	0	0	•	0		

TABLE 118 *** PATH/TOX SYSTEM OUTPUT *** SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 22-APR-88 PAGE: 81

STUDY NUMBER: 2399108 HISTOPATHOLOGY INCIDENCE SUMMARY

	HISTOPATHOLOGY INCIDENCE SUMMANY		HKY 	1			1	, ,		
1	•	N	UMB	т: 57.	- 0 F	E I	1 A	L S	-AFFECTED	
TABLE INCLUDES:	SEX	1	MALE		1	-	FEMALE	1 1		
DEATH-UNSCHED; FIND-ALL; SUBSET-ALL	GROUP:	1	-2	-3	-41	-12-		-4-		
ORGAN AND FINDING DESCRIPTION	NUMBER:	0	m į	, a	7	0 0	0 5 	4 1		
CECUM (CE)	NUMBER EXAMINED: NOT REMARKABLE:		2 2	m m	22	0	0 0	W W	,	
COLON (CO)	NUMBER EXAMINED: NOT REMARKABLE:	0 0	2 2	m jn	88	0 0	.	re re re re		
RECTUM (RE)	NUMBER EXAMINED: NOT REMARKABLE:	0 C	88	ΜM	22	90	. .	4 4 w w		
LN, MESENTERIC (MS)	NUMBER EXAMINED: NOT REMARKABLE:	00	МM	rv rv	8 8	00	00	re re	ধ ধ	
TESTIS (TE)	NUMBER EXAMINED: NOT REMARKABLE:	00	w w	n n	2.2	0 0		00	0 0	
EPIDIDYMIS (EP)	, NUMBER EXAMINED: NOT REMARKABLE:	0.0	mm	r r	2.2	00	00	00		
0UARY (0V)	, NUMBER EXAMINED: NOT REMARKABLE:	0 6	0 0	0 0	00	00	0 €	กเก	4.4	
UTERUS (UT)	. NUMBER EXAMINED: NOT REMARKABLE:	00	0 0	0	0	0 0	0 0	re re	4.4	

TABLE 11B *** PATH/TOX SYSTEM GUTPUT *** SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 22-APR-88 PAGE: 82

TSIH	HISTOPATHOLOGY INCIDENCE		SUMMARY					STUDY	STUDY NUMBER: 2399108
TABLE TARGETON		;	Σ Ο Z	B E R	- 0 -	•	Σ - z	8 - 5	ע ע ע ע ע ע ע ע ע ע ע ע ע ע ע ע ע ע ע
SEX=ALL;GROUP=ALL;SCREEN=ALL;WEEKS=ALL DEATH=UNSCHED;FIND=ALL;SUBSET=ALL	SEX:	1	MALE	E	i ! !	-	MALE		- - -
	GROUP:	-1-	-2-	€ -	-4-	-12-		-4-	
ORGAN AND FINDING DESCRIPTION	NUMBER:	0	m		2	0	0 5	4	
URINARY BLADDER (UB)	NUMBER EXAMINED: NOT REMARKABLE:		mm	44	; ; 00		0 5	i i 44	
PROSTATE (PR)	. NUMBER EXAMINED: NOT REMARKABLE:	. 0	r 6	rv 4	8 8	.	00	• 0	
MONDUCLEAR CELL INFILTRATE	•	0	1			0	0	0	
SEMINAL VESICLE (SU)	NUMBER EXAMINED: NOT REMARKABLE:		mm	R R	20	0 0	00	00	
SKIN (SK)	NUMBER EXAMINED: NOT REMARKABILE:	00	mm	2	22			44	
MAMMARY GLAND (MG)	NUMBER EXAMINED: NOT REMARKABLE:	0 0		44		0	0 0 0	mm	
MUSCLE, SKELETAL (SM)	NUMBER EXAMINED: HOT REMARKABLE:	0 0	mm	א או	2.0	9.0		44	
MERUE, SCIATIC (SN)	NUMBER EXAMINED: NOT REMARKABLE:	00	22	ህወ	2.2		0.0	44	
MAND SALIVARY GL (SG)	NUMBER EXAMINED: NOT REMARKABLE;	00	₩, ₩,	ፍራ	2.2		0 0 0 v	4 4	

TABLE 11B *** PATH/TOX SYSTEM OUTPUT *** SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 22-APR-89 PAGE: 83

HISTO	HISTOPATHOLOGY INCIDENCE SUMMARY	E SUMM	ARY	 	1 1 1 1	; ; ; ;	1	STUDY NUMBER:	R: 2399108	
	•		U M B	Ħ Я	. 0	Œ ,	Ε	LS-AFFE	.c.teo	
SEX.ALL,GROUP-ALL,GCREEN-ALL,WEEKS-ALL	SEX: -	MALE	-MALE	1 1		FE	FEMALE	!		
DEATH-UNSCHEDJFIND-ALLJSWBSET-ALL	GROUP: -	-1-	-2	-3-	-41-	-2-	-4	-4-		
ORGAN AND FINDING DESCRIPTION	NUMBER	1 0 :	, m	ן ו או	2 0	0 0	R 1	4 1		
THYMUS (TH)	NUMBER EXAMINED: NOT REMARKABLE:	0	m m	rv rc	2 2	00	re re	44		
AORTA, THORACIC (AO)	NUMBER EXAMINED: NOT REMARKABLE:	0 0	00	N N	88	90	r r	44		
EYE (EY)	NUMBER EXAMINED: NOT REMARKABLE:	90	10° 10°	44	88	00	44	44		
LACRIMAL GL, EXO (EO)	NUMBER EXAMINED: NDT REMARKABLE:	00	m m	ro ro	2.2	00	r r	4.4		
BONE, STERNUM (SB)	NUMBER EXAMINED: NOT REMARKABLE:		W W	r r	88	00	r. r.	44		
MARROW, STERNUM (SE)	NUMBER EXAMINED: NOT REMARKABLE:	00	mm	n n	22		re re	44		
BONE, FEMUR (FE)	NUMBER EXAMINED: NOT REMARKABLE:		m 0	กก	2 2	0 0	r 4	4 W	-	
ARTICULAR SURFACE NOT PRESENT		0	**	0	0	0	-			
LN, OTHER (LN)	NUMBER EXAMINED: NOT REMARKABLE:	0 0	0	00	00	00	••	• 0		
HYPERPLASIA, LYMPHGID		0	-	0	0	0 0	•	0		

TABLE 11B
*** PATH/TOX SYSTEM OUTPUT ***
SUBCHRONIC TOXICITY STUDY IN RAIS

PRINTED: 22-APR-88 PAGE: 84

STUDY NUMBER: 2399108

HISTOPATHOLOGY INCIDENCE SUMMARY

		Z	Σ Э	E 22	0	4	Σ.		ر ب
TABLE INCLUDES: SEX-ALL;SCREEN-ALL;WEEKS-ALL OCATH-INCLUDES:	SEX	SEX:MAI.E	HAH-		· '	FEMALE	EMALE-		- - - - -
	GROUP: -12341234-	-1-	-2-	Ę.	4-	12	,	-4-	
ORGAN AND FINDING DESCRIPTION	NUMBER: 6		· ·	ا	2	0 1	5 -	4	
SKIN, OTHER (SS)	NUMBER EXAMINED:	00	10		0 0	00	00	0 0	
INFLAMMATION, GRANULOMATOUS ** END OF LIST **		0	-	•	6	0	0	0	

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APPENDIX 1

Individual Animal Disposition

*** PATH/TOX SYSTEM OUTPUT *** SUBCHRONIC TOXICITY STUDY IN RAIS

INDIVIDUAL ANIMAL DISPOSITION

PRINTED: 22-APR-88 PAGE: 86

STUDY NUMBER: 2399108

ANIMAL (PIN)	AN I MAL-NUMBER (P I N) (HAN)	DOSE	SEX	TERMINAL BODY WEIGHT	DEATH CODE	TYPE OF DEATH	DESCRIPTION OF DEATH	DATE OF DEATH	DAY OF STUDY	WEEK OF STUDY
0836	863882	1		563.2	<u> </u>	SCHEDULED	TERMINAL SACREFICE	07/14/84	98	
B08363	863883	-	MALE	S	 - -	SCHEDULED		07/14/86	0.0	11
B08364	863884	, -	MALE	543.3	 	SCHEDULED	TERMINAL SACRIFICE	07/14/B6	00	4.
808365	863885	-	MALE	6.509	-	SCHEDULED	TERMINAL SACRIFICE	07/14/86	66	4.
808366	963886	-	MALE	457.0	_	SCHEDULED	TERMINAL SACRIFICE	07/14/86	95	4
B08367	863887		MALE	451.7	 	SCHEDULED		07/14/86	. 6	4
808368	863868	-	MALE	511.3	-	SCHEDULED		07/15/86	. 6	7 -
808369	863889	-	MALE	508.4	Ĺ	SCHEDUL.ED	٠.	07/15/86	96	4
B08370	863890	÷	MALE	459.9	H	SCHEDULED	TERMINAL SACRIFICE	07/15/86	96	. 4
B08371	863891	, , ,	MALE	493.7	_	SCHEDULED	TERMINAL SACRIFICE	07/15/86	96	. 4
B08372	863892	- -	MALE	487.8	_	SCHEDOLED	TERMINAL SACRIFICE	07/15/86	96	14
B08373	863893	-	MALE	588.4	_	SCHEDULED	TERMINAL SACRIFICE	07/15/86	96	4
B08374	863894	-	MALE	524.3	-	SCHEDULED	TERMINAL SACRIFICE	07/15/86	96	14
B08375	863895	-	MALE	459.3	_	SCHEDULED	TERMINAL SACRIFICE	07/16/86	9.5	14
B08376	863896	-	MALE	518.8		SCHEDITED	TERMINAL SACRIFICE	07/16/86	6	14
B08377	863897	1	MALE	492.3	-	SCHEDULED	TERMINAL SACRIFICE	07/16/86	6	14
B08378	863888	-	MALE	498.1	_	SCHEDULED	TERMINAL SACRIFICE	07/16/86	9.2	14
B08379	863899	-	MALE	494.7	- -	SCHEDULED	TERMINAL SACRIFICE	07/16/86	6	14
B08380	863900	-	MALE	554.1	-	SCHEDOLED	TERMINAL SACRIFICE	07/16/86	6	14
808381	863901	e-11	MALE	479.0	-	SCHEDULED.	TERMINAL SACRIFICE	07/16/86	97	14
BUB402	863922	7	MALE	265.5	Σ	UNSCHEDULED	UNSCHEDULED DEATH	04/23/86	13	2
B08403	863923	7	MALE	516.3	-	SCHEDULED	TERMINAL SACRIFICE	07/14/86	66	14
B08404	865924	7	MALE	512.3	-	SCHEDOLED	TERMINAL SACRIFICE	07/14/86	95	14
HU8405	863925	7	MALE	492.8	-	SCHEDOLED	TERMINAL SACRIFICE	07/15/86	96	14
BU8406	863926	2	MALE	515.8	- -	SCHEDULED		07/15/86	96	14
200407	165927	24 (HALE	481.6	_	SCHEDULED	-,	07/15/86	96	14
000400	92429	7 (MALE	473.1	-	SCHEDULED		07/14/86	95	14
000409	42.4CQA	N (TALE I	471.7	-	SCHEDULED	٠.	07/14/86	95	14
000410	062720	ν 0	TALE	492.B	- 1	SCHEDULED	•	07/14/86	95	14
111000	164600	۷ (14. F	5/5.0	-	SCHEDULEO		07/15/86	96	14
214800	862932		MALE	527.4	_	SCHEDUL ED	-:	07/15/86	96	14
505413	865955	Ν (MALE	506.0	-	SCHEDULED	٠.	02/16/86	97	14
808414	862724	.7 (MALE:	528.3	_	SCHEDULED		07/15/86	96	14
500412	6272		MALE	460.6	-	SCHEDULED	TERMINAL SACRIFICE	07/15/86	96	14
606416	865956	2 '	MALE	425.6	_	UNSCHEDULED	UNSCHEDULED DEATH	05/14/86	34	r
716909	863937	.7	MALE	S.	۵	UNSCHEDULED	UNSCHEDULED DEATH	04/25/86	15	۴
	6393	C4 1	MALE	Š	-	SCHEDULED	TERMINAL SACRIFICE	07/16/86	97	14
618419	6593	7	MALE	499.3	_ (SCHEDULED	TERMINAL SACRIFICE	07/16/86	26	14
B08420	863940	7	MALE	443.2	—	SCHEDULED	TERMINAL SACRIFICE	07/16/86	6	14
						•				

A** PATH/TOX SYSTEM OUTPUT *** SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 22-APR-88 PAGE: 87

STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL DISPOSITION

WEEK OF STUDY	14	14	14	14	14	m	14	2	. 14	8	14	14	14	۴	14	14	14	-	14	14	14	14	14	14	14	14	14	4	14	14		4	r	14	14	14	14	14	14
DAY OF STUDY	97	95	95	95	95	20	96	34	95	51	96	96	97	19	6	97	96	4	6	97	6	95	96	96	95	95	96	96	96	95	96	96	17	6	92	96	96	6	97
DATE OF DEATH	07/16/86	07/14/86	07/14/86	07/14/86	07/14/86	04/30/86	02/15/86	05/14/86	07/14/86	05/31/86	07/15/86	07/15/86	07/16/86	04/29/86	07/16/86	07/16/86	07/15/86	04/14/86	07/16/86	07/16/86	07/16/86	07/14/86	07/14/86	07/14/86	07/14/86	07/14/86	07/14/86	02/15/86	07/15/86	07/14/86	98/40/90	07/15/86	04/27/86	07/16/86	07/16/86	07/15/86	07/15/86	07/16/86	07/16/86
DESCRIPTION OF DEATH	TERMINAL SACRIFICE					_	TERMINAL SACRIFICE		TERMINAL SACRIFICE		TERMINAL SACRIFICE	TERMINAL SACRIFICE	TERMINAL SACRIFICE	UNSCHEDULED DEATH	TERMINAL SACRIFICE			-	TERMINAL SACRIFICE	TERMINAL SACRIFICE			TERMINAL SACRIFICE	UNSCHEDULED DEATH	TERMINAL SACRIFICE	UNSCHEDULED DEATH	TERMINAL SACRIFICE		TERMINAL SACRIFICE			TERMINAL SACRIFICE							
TYPE OF DEATH	CCHEDIII ED	SCHEDIII ED	SCHEDILL ED	SCHEDIA FO	SCHEDIII ED	INSCHEDIN FO	SCHEDIA FO	INSCHEDIN FO	SCHEDIII FO	INSCHEDIT ED	SCHEDIA FD	SCHEDULED	SCHEDILLED	INSCHEDULED	SCHEDITED	SCHEDIE FD	SCHEDINED	INSCHEDIT ED	SCHEDULED	SCHEDULED	SCHEDULED	SCHEDIII ED	SCHEDILL ED	SCHEDULED	INSCHEDILED	SCHEDUL ED	UNSCHEDUL ED	SCHEDIL ED	SCHEDUL ED	SCHEDI LED	SCHEDIN FD	SCHEDULED	SCHEDUL ED						
DEATH CODE	-	- -	- 1-	- +	- 1-	- c	+ د	- c	۱ د	- c) þ.,	- ۱	- 1		-	. +	<u>-</u>	. د) -	- 1	- J	- -	. ⊢		-	- -		• 🛌	-	. -		-	· c	· -	- ب	. ⊨	-	- -	-
TERMINAL BODY WEIGHT		V: 114	474.4	1.104	700.0	422.1	7.017	400.7	702.4	45.0.5	7,00,0	3.75. 7.83. A	0.557	333.8	663.3	, 40×	510 0	216.1	7 269	7 405 7	503 6	6.797 F 444	452 5	451 8	359.5	6 444	431 B	374.9	373.1	405.0	287 1	435 9	317.0	415.0	3.71	6.00	7.077	44/./	433.5
SEX	1 - 1	7 T	1 1 1 1 1	1 H.	1 K	# 14 F	H 7	HE Y	1 K	J I	1 L	M 10 M	MOLE	M F	1 10 X		<u> </u>	1 L	MAIN P	M 10	1 L	1 1 T	MA MA M	Į L	1 I	Į Į	N I	MAIF	Į Į	M P	100	i i	NO F	1 L	MOLE	1 2	1 7	1 to	MALE
DOSE GROUP	1	7 1	٠ t	۱ ۸	n 1	۸ ۱	n 1	۱ ۱	n 1	^ P	` F	\ M	۱ ۳	٧ ٣	۱ ۲	\ P	, , ,	۱,	\ H	۱ ۳	N 14	٠, ٧	* <	7 4	1 <	r ×	* *	1 4	* *	* <	۲ ٦	*	* <	1 4	Γ <	1 4	4 4	1 4	1.4
NUMBER (HAN)	1 4 1 1	865941	863962	863963	865964	863965	863966	865967	862968	867767	0/4/08	1///08	7///00	7///00	003774	0/1/2	0/4/0R	////00	0/4/08	4/4/00	862780	196770	2004002	004100	504004	700770	004000	20400	00000000	964007	077070	004011	710400	710770	110770	804017	864010	710408	864019
ANIMAL-NUMBER (PIN) (HAN)	1 1	808421	808442	B08443	B08444	B08445	B08446	B08447	B08448	BU8449	B08458	BU8451	200427	000477	BUB474	806477	HU6450	500457	B08428	000427	000400	B08461	200407	000000	5000434	000407		000407	0004000	000000	000400	506471	5000472	5000497	100000	B08499	H08496	1808497 1007000	B08499

*** PATH/TOX SYSTEM DUTPUT *** SUBCHRONIC TOXICITY STUDY IN RATS

INDIVIDUAL ANIMAL DISPOSITION

PRINTED: 22-APR-88 PAGE: 88 STUDY NUMBER: 2399108

WEEK OF STUDY		1 T	<u> </u>	7 7		<u> </u>	<u>.</u>		7.	. 4	4	4.	14	14	14	14	14	. 41	14	14	14	14	14	14	14	14	14	14	14	14	14	14	14	14	14	7	. 4		14
DAY OF STUDY		\ 0 0	9.	0 0	. 6	95		9 6	95	. 6	96	96	6	6	96	96	96	6	9.2	6	6	26	96	95	95	95	66	95	96	96	96	96	65	96	96	0.0	6	70	9.6
DATE OF DEATH	07/1/0/	07/16/86	02/14/86	07/14/86	07/14/84	07/14/86	02/15/84	07/14/86	07/14/86	07/15/86	07/15/86	07/15/86	07/16/86	07/16/86	07/15/86	07/15/86	07/15/86	07/16/86	07/16/86	07/16/86	07/16/86	07/16/86	07/14/86	07/14/86	07/14/86	07/14/86	07/14/86	07/14/86	07/15/86	07/15/86	07/15/86	07/15/86	07/16/86	07/15/86	07/15/86	07/16/86	07/16/86	02/15/86	17/16/86
DESCRIPTION OF DEATH	TREMINAL GARAITETES		TERMINAL SACRIFICE		TERMINAL SACRIFICE		TERMINAL SACRIFICE		TERMINAL SACRIFICE	TERMINAL SACRIFICE	-	TERMINAL SACRIFICE	TERMINAL SACRIFICE		-			1		٠,		٠.	1		•							٠,	-	TERMINAL SACRIFICE	TERMINAL SACRIFICE	TERMINAL SACRIFICE		TERMINAL SACRIFICE	
TYPE OF DEATH	SCHEDIA ED	SCHEDULED	SCHEDULED	SCHEDULED	SCHEDULED	SCHEDUL.ED	SCHEDULED	SCHEDULED	SCHEDULED	SCHEDULED	SCHEDULED	SCHEDULED	SCHEDULED	SCHEDULED	SCHEDULED	SCHEDULED	SCHEDULED	SCHEDULED	SCHEDULED	SCHEDULED	SCHEDULED	SCHEDULED	SCHEDULED	SCHEDULED	SCHEDULED	SCHEDULED	SCHEDOLED	SCHEDULED	SCHEDULED	SCHEDULED	SCHEDULED	SCHEDULED	SCHEDITED	SCHEDULED	SCHEDULED	SCHEDULED	SCHEDIJLED	SCHEDULED	SCHEDULED
DEATH CODE	-	-	-	 	_	-) -	۰	_	 - -	F	-	_	-	-)	_	_	-	- 1	⊢ i	– 1	- 1)-	- 1	ļus	_	- !	- 1	- 1	- (_	-	_	_	-	-	-	⊢
TERMINAL BODY WEIGHT	443	428.0		247.1	297.1	262.4	243.6	257.0	251.2	267.0	261.7	277.8	294.7	766.0	242.5	269.5	248.6	271.1	225.8	290.1	248.3	262.3	260.3	259.0	2/2.9	261.3	256.1	275.2	2/2.9	9.997	7.622	ͺ.	•		243.1		257.5	243.2	
SEX	MALE	MALE	FEMALE	FEMALE	FEMALE	FEMALE	FEMALE	FEMALE	FEMALE	FEMALE	FEMALE	FEMALE	FEMALE	FELIFICE	FEMALE	FEMALE	FEMALE	FEMALE FILE	FEMALE	FEMALE			FETHER	FEMALE	FEITHE	FEMALE	FEMALE	FEMALE			FEIGHLE	FEFF	FEMALE	FEMALE	FEMALE	FEMALE	FEMALE	FEMALE	FEMALE
DOSE	4	4	-		-	-	-		-	-	. .	٠ .	•	٠, ٠	→ .	۰,	e4 a	۰,	۰.	٠.	→ +	⊣ (۷ (N 6	۷ (ν (۷.	N 0	۷ .	۷ (٧	v 0	N (N (N 1	2	~	7	7
ANIMAL-NUMBER (PIN) (HAN)	864020	864021	863902	863903	863904	863905	863906	863907	865908	863909	863910	114699	21,429,0	77.70	007714	014000	07 4 C 0 C C C C C C C C C C C C C C C C C	71,400	802718	003717	02//00	17//00	76//00	044040	007744	007747	01/100	070770	967948	747700	067750	16//00	26220	007700	07704	862727	863956	863957	8636598
ANIMAL- (PIN)	B08508	608501	808382	808383	B08384	808385	B08386	58585	986808	684808	066808	1/000	746900	701000	200700	70,000	000000	747000	000000	000700	B08400	104000	775000 FC7800	000427	000,000	67500 BUB424	000470	775000	B08420	77,000	B08470	1/1000	764000	000423	1474000	B08425	B08436	/\$PRA9	B08438

*** PATH/TOX SYSTEM OUTPUT *** SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 22-APR-88 PAGE: 89

STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL DISPOSITION

WEEK OF STUDY	14	14	14	14	14	14	14	13	14	m	14	14	14	14	8	14	14	4	14	2	14	14	14	14	14	14	2	14	14	14	. 14	14	14	14	14	11	64	14	14	ı
DAY OF STUDY	6	6	. 97	95	95	66	95	88	95	18	9	96	96	6	æ	96	97	96	96	18	96	97	97	95	95	ф. Ф.	11	95	95	96	96	96	96	6	97	12.	10	96	96	1
DATE OF DEATH	07/16/86	07/16/86	07/16/86	02/14/86	07/14/86	07/14/86	07/14/86	98/20/20	07/14/86	04/28/86	07/14/86	07/15/86	07/15/86	07/16/86	04/18/86	07/15/86	07/16/86	07/15/86	07/15/86	04/20/86	07/15/86	07/16/86	07/16/86	07/14/86	07/14/86	07/14/86	04/21/86	07/14/86	07/14/86	07/14/86	07/15/86	07/15/86	07/15/86	07/16/86	07/16/86	06/20/86	04/20/86	02/15/86	07/15/86	
DESCRIPTION OF DEATH	TERMINAL SACRIFICE		TERMINAL SACRIFICE	UNSCHEDULED DEATH	TERMINAL SACRIFICE	UNSCHEDULED DEATH	TERMINAL SACRIFICE	TERMINAL SACRIFICE	TERMINAL SACRIFICE	TERMINAL SACRIFICE	UNSCHEDULED DEATH	TERMINAL SACRIFICE	TERMINAL SACRIFICE	TERMINAL SACRIFICE	TERMINAL SACRIFICE	UNSCHEDULED DEATH	UNSCHEDULED DEATH	TERMINAL SACRIFICE	UNSCHEDULED DEATH		TERMINAL SACPIFICE	TERMINAL SACRIFICE	UNSCHEDULED DEATH	UNSCHEDULED DEATH	TERMINAL SACRIFICE															
TYPE OF DEATH	SCHEDINED	SCHEDULED	SCHEDULED	SCHEDULED	SCHEDULED	SCHEDULED	SCHEDULED	UNSCHEDULED	SCHEDULED	UNSCHEDULED	SCHEDULED	SCHEDULED	SCHEDULED	SCHEDULED	UNSCHEDULED	SCHEDULED	SCHEDULED	SCHEDULED	SCHEDULED	UNSCHEDULED	UNSCHEDULED	SCHEDULED	SCHEDOLED	SCHEDULED	SCHEDULED	SCHEDULED	UNSCHEDULED	SCHEDULED	SCHEDULED	SCHEDUR ED	SCHEDULED	SCHEDULED	SCHEDULED	SCHEDULED	SCHEDULED	UNSCHEDULED	UNSCHEDULED	SCHEDULED	COHEDINE	J. (15)/(11)
DEATH CODE	<u> </u>	· þ.	-	-	-	-	–	٥	_	٥	-	-	⊢	_	۵	-	-	_	_	٥	۵	-	-	-	-	-	٥	_	-	-	-	-	;	-	}	۵	۵ ۵	-	- +	-
TERMINAL BODY WEIGHT	261.4	253.9	254.6	247.8	236.6	239.5	249.3	280.5	257.2	201.3	258.1	236.9	249.4	290.1	165.7	249.0	258.1	269.2	275.9	180.2	242.1	257.7	259.0	259.9	235.2	228.2	175.2	230.9	258.4	233.2	227.0	211.9		265.8	236.4	251.9	178.0	2,65.2	1. 100	n·/77
SEX	FEMALE	FEMAI F	FEMALE	FEMALE	FEMAI E	FEMALE	FEMALE	FEMALE	FEMALE	FEMALE	FEMALE	FEMALE	FEMALE	FEMALE	FEMALE	FEMALE	FEMALE	FEMALE	FEMALE	FEMALE	FEMALE	FEMALE	FEMALE	FEMALE	FEMALE	FEMALE	FEMALE	FEMALE	FEMALE	FEMALE	FEMALE	FEMALE	FEMAI F	FEMAI F	FEMAI F	FFMAIF	FEMAI F	FFMOLF	() () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () () ()	FETHLE
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ANIMAL-NUMBER (PIN) (HAN)	040740	863960	863961	863982	863983	863984	863985	8639R6	863987	8639BB	863989	863990	863991	863992	863993	863994	863995	863996	863997	R63998	863999	864000	864001	864022	864023	864024	864025	864026	864027	864028	864029	R64030	864031	B64032	864033	B64034	964035	064034	001000	H64U2/
ANIMAL- (PIN)	017000	B08457	B18441	B08442	B08463	B08464	B08454	HORASA	B08467	B08468	B08469	B08420	808471	B08472	B08473	B08474	R08475	B08476	B08477	B08478	H08479	B08480	B08481	B08502	B18503	B08504	808505	808506	B08507	B08508	ROR509	B08510	908511	B08517	5000	B08514	B08514	0000	01/000	H0851/

*** PATH/TOX SYSTEM DUTPUT *** SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 22-APR-88 PAGE: 90

INDIVIDUAL ANIMAL DISPOSITION

STUDY NUMBER: 2399108

EATH DEATH STUDY S	EATH DEATH STUDY 0EATH STUDY 07/16/86 97 05/16/86 97 07/16/86 97	DEATH TYPE OF DESCRIPTION OF DEATH DEATH STUDY	DEATH TYPE OF DESCRIPTION OF DEATH DEATH STUDY	TYPE OF DESCRIPTION OF DEATH DEATH STUDY	DOSE TERMINAL DEATH TYPE OF DEATH DEATH DEATH DEATH DEATH STUDY GROUP SEX BODY WEIGHT CODE DEATH DEATH STUDY 4 FEMALE 239.8 T SCHEDULED TERMINAL SACRIFICE 07/16/86 97 4 FEMALE 214.2 D UNSCHEDULED TERMINAL SACRIFICE 07/16/86 97 4 FEMALE 258.6 T SCHEDULED TERMINAL SACRIFICE 07/16/86 49	SEX BODY WEIGHT CODE DEATH TYPE OF DESCRIPTION OF DEATH DEATH STUDY FEMALE 239.8 T SCHEDULED TERMINAL SACRIFICE 07/16/86 97 FEMALE 214.2 D UNSCHEDULED TERMINAL SACRIFICE 07/16/86 97 FEMALE 258.6 T SCHEDULED TERMINAL SACRIFICE 07/16/86 49	70	≿	Į.	l i					
DATE OF EATH DEATH 07/16/86 07/16/86 07/16/86 07/16/86	DESCRIPTION OF DEATH DEATH TERMINAL SACRIFICE 07/16/86 UNSCHENKED DEATH 05/29/86 TERMINAL SACRIFICE 07/16/86	DEATH TYPE OF DESCRIPTION OF DEATH DEATH	DEATH TYPE OF DESCRIPTION OF DEATH DEATH	TERMINAL DEATH TYPE OF DESCRIPTION OF DEATH	DOSE TERMINAL DEATH TYPE OF DEATH	DOSE TERMINAL DEATH TYPE OF DEATH	LF.EX	STUC	1	-	1 ,	7	•	• ;	4
EATH [DESCRIPTION OF DEATH TERMINAL SACRIFICE TERMINAL SACRIFICE UNSCHENLED DEATH TERMINAL SACRIFICE	DEATH TYPE OF CODE DEATH DESCRIPTION OF DEATH T SCHEDULED TERMINAL SACRIFICE T SCHEDULED TERMINAL SACRIFICE D UNSCHEDULED TERMINAL SACRIFICE T SCHEDULED TERMINAL SACRIFICE T SCHEDULED TERMINAL SACRIFICE T SCHEDULED TERMINAL SACRIFICE	DEATH TYPE OF CODE DEATH DESCRIPTION OF DEATH T SCHEDULED TERMINAL SACRIFICE T SCHEDULED TERMINAL SACRIFICE D UNSCHEDULED TERMINAL SACRIFICE T SCHEDULED TERMINAL SACRIFICE T SCHEDULED TERMINAL SACRIFICE T SCHEDULED TERMINAL SACRIFICE	TERMINAL DEATH TYPE OF DESCRIPTION OF DEATH DEATH DEATH DEATH DESCRIPTION OF DEATH D	DOSE TERMINAL DEATH TYPE OF GROUP SEX BODY WEIGHT CODE DEATH DESCRIPTION OF DEATH CODE DEATH CODE CODE DEATH CODE CODE	DOSE TERMINAL DEATH TYPE OF GROUP SEX BODY WEIGHT CODE DEATH DESCRIPTION OF DEATH CODE DEATH CODE CODE DEATH CODE CODE	DAY OF	STUDY		0.7		\ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \	67	÷ (`
DESCRIPTION OF DEATH TERMINAL SACRIFICE TERMINAL SACRIFICE UNSCHEDULED DEATH TERMINAL SACRIFICE	. — .	DEATH TYPE OF CODE DEATH T SCHEDULED T SCHEDULED D UNSCHEDULED T SCHEDULED	DEATH TYPE OF CODE DEATH T SCHEDULED T SCHEDULED D UNSCHEDULED T SCHEDULED	TERMINAL DEATH TYPE OF BODY WEIGHT CODE DEATH 239.8 T SCHEDULED 284.1 T SCHEDULED 214.2 D UNSCHEDULED 258.6 T SCHEDULED	DDSE TERMINAL DEATH TYPE OF GROUP SEX BODY WEIGHT CODE DEATH 4 FEMALE 239.0 T SCHEDULED 4 FEMALE 214.2 D UNSCHEDULED 4 FEMALE 214.2 D UNSCHEDULED 4 FEMALE 258.6 T SCHEDULED	DDSE TERMINAL DEATH TYPE OF GROUP SEX BODY WEIGHT CODE DEATH 4 FEMALE 239.8 T SCHEDULED 4 FEMALE 214.2 D UNSCHEDULED 4 FEMALE 214.2 D UNSCHEDULED 4 FEMALE 258.6 T SCHEDULED	DATE OF	DEATH	1 1 1 1	87/14/84	20,71,70	6// 10/00	05/29/84		16/86
	TYPE OF DEATH SCHEDULED SCHEDULED UNSCHEDULED SCHEDULED UNSCHEDULED SCHEDULED	DEATH CODE T T T T	DEATH CODE T T T T	TERMINAL DEATH BODY WEIGHT CODE	DOSE TERMINAL DEATH GROUP SEX BODY WEIGHT CODE 4 FEMALE 239.8 T 4 FEMALE 214.2 D 4 FEMALE 214.2 D 4 FEMALE 258.6 T	GROUP SEX BODY WEIGHT CODE		DESCRIPTION OF DEATH		TERMINAL SACRIFICE	TEDMINAL CAPOTETOR		UNSCHEINED DEATH	TOTAL TOTAL TOTAL	

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APPENDIX 2 Individual Clinical Observations

APPENDIX 2 INDIVIDUAL CLINICAL DESERVATIONS 2399-108

			·	
	GROUP	ANIMAL	CLINICAL	BODY
MEEK	& SEX	NUMBER	OBSERVATION	AREA
. 0	2H	8402	SORES	NECK
1	2M	8402	SORES	NECK
	4M	8494	BLOGDY CRUST	NOSE
	4M	8475	SORES	NECK
3	1M	8379	BLOODY CRUST	HEAD
	4M	8484	URINE STAINS	ABDOMEN
6	4M	8487	URINE STAINS ALOPECIA	INGUINALS-BOTH ABDOMEN
	4M	8490	URINE STAINS	INGUINALS-BOTH
	4M	8494	SMALL MOVEABLE TISSUE MA	INGUINALS-BUIN SC USNIBL-ST BOUT
7	4M	8494	SMALL MOVEABLE TISSUE MA	SC UENTS ET BOUT
8	1M	8371	MALOCCLUSION	135 VENIKE-FI-KGHI
		· -	CHROMODACRYORRHEA	EYE-LEFT
	1M	8372	MALOCCLUSION	E (E - LEF)
	3M	8453	MALOCCLUSION	
	3M	8455	CHROMODACRYGRRHEA	EYE-RIGHT
	4H	8483	CHROMODACRYORRHEA	EYE-RIGHT
	4M	8487	ALOPECIA	INGUINAL-LEFT
	4M	8494	SMALL MOVEABLE TISSUE MA	
9	1M	8371	TEETH CUT	SS VENIKL-FI-KGRI
			CHROMODACRYORRHEA	EYE-LEFT
	1M	8372	TEETH CUT	C1E-CEF1
			CHROMODACRYORRHEA	EYE-RIGHT
	1M	8377	TEETH CUT	E I E - K I GFI I
	2M	8420	TEETH CUT	
	3M	8447	TEETH CUT	
			MALOCCLUSION	
			CHROMODACRYORRHEA	EYES-BOTH
	ЗM	8453	TEETH CUT	· · · · · · · · · · · · · ·
	3M	8455	TEETH CUT	
	4M	8483	CHROMODACRYORRHEA	EYE-RIGHT
	4M	8484	URINE STAINS	SCROTUM
	4M	8494	SMALL MOVEABLE TISSUE MA	
10	1M	8371	TEETH CUT	oo vanne i kann
			CHROMODACRYORRHEA	EYE-LEFT
	2M	8404	TEETH CUT	
	2M	8413	TEETH CUT	
	2M	8415	TEETH CUT	
	2M	8420	MALOCCLUSION	
	3M	8447	MALOCCLUSION	
			CHROMODACRYORRHEA	EYE-RIGHT
	3M	8452	TEETH CUT	E.E NIGHT
	ЗM	8453	TEETH CUT	
	3M	8455	TEETH CUT	
			CHROMODACRYORRHEA	EYE-RIGHT
	ЗM	8459	TEETH CUT	C.C.KIGU!
	4M	8483	. TEETH CUT	
			· · · · · · · · · · · · ·	

APPENDIX 2 INDIVIDUAL CLINICAL OBSERVATIONS 2399-108

	GROUP	ANIMAL	CLINICAL	BODY
MEEK	& SEX	NUMBER	OBSERVATION	AREA
10	4M	8483	CHROMODACRYORRHEA	EYE-RIGHT
	4M	8492	TEETH CUT	-
	4M	8494	SORES	AXILLA-RIGHT
11	1 M	8371	TEETH CUT	
			CHROMODACRYORRHEA	EYE-LEFT
	1M	8372	TEETH CUT	
-	2M	8411	TEETH CUT	
			CHROMODACRYORRHEA	EYE-RIGHT
	2M	8420	TEETH CUT	
	3M	8447	TEETH CUT	•
	•	_ , , ,	MALOCCLUSION	
	3M	8455	TEETH CUT	
	4. .	0 100	CHROMODACRYORRHEA	EYE-RIGHT
	3M	8459	TEETH CUT	
	4M	8483	1EETH CUT	
	•••	2 .23	CHROMODACRYORRHEA	EYE-R1GHT
13	1M	8367	CHROMODACRYORRHEA	EYE-RIGHT
	1M	8371	MALOCCLUSION	
			CHROMODACRYORRHEA	EYE-LEFT
	2M	8411	MALOCCLUSION	
		U -104	CHROMODACRYORRHEA	EYE-RIGHT
	2M	8420	MALOCCLUSION	<u></u>
	3M	8447	MALOCCLUSION	
	3M	8455	CHROMODACRYORRHEA	EYES-BOTH
	4M	8483	CHROMODACRYDRRHEA	EYE-RIGHT
	4M	8487	BLOODY CRUST	NOSE
	711	0407	CHROMODACRYORRHEA	EYE-RIGHT

APPENDIX 2
INDIVIDUAL CLINICAL OBSERVATIONS
2399-108

	GROUP	ANIMAL	CLINICAL	BODY
MEEK	& SEX	NUMBER	OBSERVATION	AREA
2	1F	8400	SORES	NECK
3	1F	8400	SORES	NECK
6	4F	8507	URINE STAINS	
•	4F	851 <i>0</i>	URINE STAINS	INGUINALS-BOTH
i	4F	8513	SALIVATION	INGUINALS-BOTH
	4F	8516		THOUTHALD DOT!
		8517	URINE STAINS	INGUINALS-BOTH
_	4F		URINE STAINS	INGUINALS-BOTH
7	4F	8510 8510	URINE STAINS	INGUINALS-BOTH
8	1F	8385	SORES	HEAD
_	3F	8471	ALOPECIA	LEGS-FORE-BOTH
9	1F	8384	TEETH CUT	
			MALOCCLUSION	•
			CHROMODACRYORRHEA	EYES-BOTH
	3F	8476	TEETH CUT	
18	1F	8384	TEETH CUT	
	1 F	8394	TEETH CUT	
	2F	8439	TEETH CUT	
	3F	8465	ALOPECIA	LEG-FORE-RIGHT
	3F	8471	ALOPECIA	LEGS-FORE-BOTH
	4F	8516	ALOPECIA	LEGS-FORE-BOTH
	4F	8517	TEETH CUT	
11	1F	8384	TEETH CUT	
	1F	8391	TEETH CUT	•
			BLOODY CRUST	NOSE
			CHROMODACRYDRRHEA	EYE-LEFT
	3F	8465	ALOPECIA	HEAD
12	1F	8391	BLOODY CRUST	EYE-LEFT
13	1F	8384	MALOCCLUSION	
			CHROMODACRYORRHEA	EYE-RIGHT
	4F	8513	SALIVATION	
	1,	~~~~	Orima viti a Oit	

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APPENDIX 3
Individual Body Weights

13		92.	469.3	. 0		7.	ξ.	27.	4.	= :	9:		֝ ֖֖֓֞֝֞֝֓֓֓֓֓֞֝֝֓֡֓֞֝֓֡֓֓֡֝֝֓֡֓֡֡֝		6	9	4	76.	12.		*		527.5												*	52.	514.5	62.	<u>.</u>
12		582.2	5471.5																		*	531.5	528.9	513.5	536.0	504.2	498.2	496.9	544.2	7,076	500.4	5,46	477.6	*	*	39	513.6	5	٥.
7																					*	522.0	515.9	502.0	523.8	498.9	486.6	484.4	529.2	787.8	740.7	528.0	464.9	*	*	29.	5.905	42.	
10		548.8	457.B																		*		505.5												*	4.	490.B	ċ	•
6		525.9	448.8	571.9	462.4	484.8	504.5	477.1	459.0	468.6	469.B	521.4	466.7	503.1	473.1	491.7	478.1	533.1	463.5		*		491.2												*	_	479.6		_
8		507.9	400.7	. 6		_:	<u>~</u>	Υ.	÷	٠.		٠.	:				_:	٠.	Α.		*		473.6												*	M	465.1	Ŗ	œ
7		487.7	417.7	524.5	435.5	451.4	473.2	462.7	436.2	466.5	447.6	710.7	411.9	467.1	442.5	467.5	453.7	494.1	437.5		*		458.6			-		-	-	-	-			-	*	Ψ.	443.3	6	w.
WEEKS 6		461.8	2 e	: -:							420.1					-					*	443.0	435.5	402.8	440.7	417.9	431.0	418.8	460.1	467.0	40.6	445.B	404.7	*	*		431.8	96.	
2		428.4	420.5	470.6	382.3	405.0	431.4	416.2	401.6	415.6	374.6	4/7.1	378.1	436.5	400.8	419.5	411.1	448.3	403.0		*	417.8	406.9	375.1	416.8	391.4	403.1	391.0	422.5	474.7	386 9	435.7	383.0	*	*	Ε.	416.6	Š.	4.
4		408.4	407. B	447.8	381.7	394.2	412.0	396.4	382.3	407.9	2//.1	411.7	361.6	408.7	376.7	398.0	388.7	419.5	378.3		*	m	393.3	Š.	9	4.	<u>م.</u> ا	∹.	. ·	· -				ö	*	95.	390.2	63.	39.
3		371.1					•													10 MG/KG	*	61.	369.2	34.	64.	38	. 61	4.0			30.	7	36.	89.	*	56.	359.5	35	14.
2	CONTROL	334.3	ے ن	Ċ	Ξ.	ĸ.	4.	ĸ.	ĸ,	Š	Ċ	: -	'n	Α,	κ.	m.	_:		۲.	100.000	*	26.	336.6	90	28.	95.	25.	2	, k	30.	96	39.	01.	42.	14.	15.	22.	01.	
	•	285.7																		ا چ			289.9										_	-	_				
0	1 MALES	235.6																_	-	2 MALE!			234.7																
AN I MAL NUMBER	GROUP	8362	- M	m	8366	m	m	m 1	~ .	МΝ	~ r	· *		•	ж.	M	•	₩.		GROUP	40	5	8404	3	6 .	2 5	. 4	₹ 7	7 7	1.2	41	41	41	41	41	4.1	7	3 9	5

APPENDIX 3 - CONTINUED INDIVIDUAL BODY WEIGHTS (G) SUBCHRONIC TOXICITY IN RATS

PAGE 97 HLA 2399108

ANIMAL	0	1	2	3	4	5	WEEKS 6	,	8	6	10	11	12	13
GROUP	3 MALE	ES -	200.0000	10 MG/KG										
8442		277.5	Κ,	346.5	58	•		404.9	_	435.7	450.8	462.9	69	466.2
8443	218.9	265.8	304.4	333.8	359.0	381.2	398.7	426.8	3	457.6	479.3	486.4		÷.
8444		283.6	ς.	361.0	96	4	٠.	-	P	482.6	-	507.2	9 [•
8445	-	282.6	ς:	346.9	7	_			32	445.7	- '	46y.	$\langle \cdot \rangle$: 1
8446	-	277.3	ä					*	*	- 1		* (* c
8447		288.0	Κ,		8	418.1	450.7	466.8	484.5	470.9	484.5	488.1	495.1	472.7
8448		276.0	۲.		3	•			- 1	* ;		٠,		٧
8449		250.0	٠.	313.7	۵.	348.8	371.5	391.8	400.3	416.8	421.5	4.4	448.8	444.7
8450		275.7	٠.		8	-	m i	OT 1	* ,	٠,	• (٠,		* 077
8451		259.2	ď		2		Λ.	IO (406.5	4.		Œς		400.7
8452		276.4	'n		2		9	~	422.6	450.7	452.U	460.7	474.4	447.7
8453		271.5	ď.		ξ.		О .	←	421.7	38.		466.5	. 1	478. I
8454		283.1				*			1	•	٠,	•	• 2	
8455		271.9	٠.	334.9	372.0	397.9	ė.	434.6	440.2	461.0	۸ I	→ 0	۰ ٥	0.104
8456		290.1	ıc'		ŏ	è	6	í.	470.3			٠	9	4
8457		274.4	ö	4	8	ö	36.	•	474.8		_;	E	Э.	
8458		*		*	*	*		*	*	*	*	*	*	* !
8459			Κ.	ъ.	83.	12.	•	2	3,4	7	81	495.5	508.0	517.8
8460		275.5	316.8	350.6	378.7	484.7	421.3	•	٠.		'n.	· ·	::	Ε,
S		281.3	9	357.2	80.	12.	ä	41.	50.		86.	ď	13.	24.
GROUP	4 MALE	ES	800.0000	OO MG/KG										
8482			25.	42.		397.1	421.6	436.1		m	472.3	484.9	500.2	490.5
8483				56.		396.0	421.6	409.8		۲.		460.4	480.8	
48				00		367.4	387.7	397.0		œ.		428.3	443.0	
48				93.		328.9	344.7	345.3		-		380.7	389.0	
9486				22.		366.5	384.9	407.4	424.9	428.7	446.2	464.1	479.2	474.0
8487				49.		373.3	394.4	404.1		ď		455.0	463.2	
8488				20.		346.7	379.3	398.0		<u>.</u>	401.1	415.1	282.1	
8489				52.	•	313.3	349.1	358.6	•	٠ ن م		277.5	405.2	
8490				æ	334.7	343.8	367.0	375.0		\sim	. 1	420.1	. 1	
8491				12.		344.6	369.5	349.6		* (•	i	- ;	
8492				35.	•	392.3	412.0	400.3	410.5	422.9	444.4	451.2	462.2	400.0
8493				*			*	*	* ;	*	* (* r		* '
8494	•			91.	20	51		384.1			408.1	427.1	- L	444.
8495	•			99.	34	54		370.5	83		402.8	420.5	٠.	424.7
8496				27.	63	8		430.7	44		455.7	467.5	٠,	4/1.7
8497				34.	99	90		422.0	5		443.1	456.9		20. 20. 20.
8498				29.	65	65		401.0			445.1	471.6		4.4.4
8499				24.	4	92		421.8	31.		446.5	469.0		424.4
8500	219.0	263.1	292.4	323.3	354.5	373.3	404.2	407.6	426.4	429.8	453.1	454.6	46U.B	468.5
8501				09.	46	64		382.3	92.		416.B	476.2		401.0

ANIMAL							WEEKS							
NUMBER		-	2	2	4	2	9	7	8	8	13	=	12	13
GROUP	1 FEM	FEMALES -	CONTROL											
3	159.3		199.	8				266.1	71.	277.4	%			
36	157.3		190.	9				235.9	36.	249.4	59.			
~ `	164.6		200.	6			-	287.1	4.	281.3	99.			
8383	161.7	186.6	205.0	213.0	216.8	236.1	247.6	249.3	250.3	263.1	269.3	272.1	270.2	268.1
, <u>s</u>	164.4		1001	ŗ				222.7	-	242.0				
388	165.1		284.	. 9				23.6	, a	262.5	₹2			
36	165.6		210.	23				284.9	2	279.8	. 4			
39	155.9		196.	16.				253.5	. 0	266.4				
3	169.3		213.	62			_	291.3	4	303.7	0			
3	162.7		206.	ž.			-	263.7	Ö.	298.1	25.			
8	158.9		205.	=			-	247.4	<u>.</u>	260.7	5.			
33	160.1		195.	9				234.2	32.	235.4	ž			
2	163.8		205.	$\frac{7}{2}$				251.8	8.	276.5	20.			
Ž. 1	163.7		194.	9				246.7	ĕ.	258.1	50.			
Ž.	154.0		197.	9				253.3	53	268.5	7:			
2 (158.6		192.	7				219.7	21.	234.2	37.			
, .	170.5		225.	4				289.7	35.	295.6	3.			
⊋ (155.4		195.	9			238.5	240.2	2	266.5	51.			
⊋	173.4		210.	33.				256.9	8	271.5	71.			
GROUP	2 FEMALI	ALES -	100.00	00 MG/KG										
42	56.		283.	15.	4.		M		٠,	κ,	-	71.		78.
42	54.		192.	13.	ĸ.	m.	ь.		ď	<u>.</u>	N	69		69
4.5	63		201.	18.	φ.	Κ.	æ.		ς.	ď	Ξ.	6.		84.
3,	?		203	7	٠.	œ.	œ.		÷	ď.	ö	8		80.
3,	5,		187.	96.	<u>.</u>	≟.	9		Š		٠.	58.		50.
3 5	40.4	-	217.	ζ,	a r	٠.	Κ,		٠.	<u>.</u>	ö	Š.		97.
8429	161.2	190.7	212	230.6	23/.2	222.7	233.7	276.9	26/.5	268.1	269.0	279.8	293.8	289.0
43	56.		193.	95.	: -	: ~:			: <	: _:		. 5		45.
53	65.	-	205.	26.	Κ.	~:	6		· .:	: -:				65.
4	. 69		195.	01.	ς.	.	ď		_:	Α.	ĸ.	53		66.
Ž,	59		201.	16.	×:	÷	'n.		٠.	٠.	9	72.		98
3 ,	<u>`</u> ;		186.	9.5	≟.	٠.	ĸ.		÷	÷	4	55.		54.
3 4	9 9	_	195.	. 6	٠.	ႊ.	ď		٠.		ĸ.	9.		63.
3 4	, , ,	_	193		ά,	٠.	Κ.			٠.	\vec{k}	53.		80.
7 5	, ,	_		4 0	٠.	٠.	٠.		<u>.</u>	٠.	ĸ.	41.		57.
, M	4.1	_	176.	N C	• 1	_; ,	<u>.</u>			٠.	m.	32		95.
1 3		-	200.		٠,	٠.	٠,		٠,	ᆣ.	i	58		٤.
7 7			201.		0.717	٠.	٠,	235.6	247.0	258.4	ĸ,	252.6		75
Ţ			700.			٠.			•	267.4	ĸ.	9.		75.

ANIMAL	0		2	3	4	7.	WEEKS 6	7	63	9	10	1	12	13
GROUP	3 FEMALE	HES -	200.000	10 MG/KG										
8462	64.	86.	98.	_		1	237.7	243.2	254.1	256.5	57.	φ.	267.4	263.3
8463	52.	73.	8.	•	•		225.6		_	246.0	4.	ζ.,	ζ.	
8464	52.		91.	_	_	10	231.6	-	_	245.9	4.	4.	. [9	-
8465	99		91.	207.2	203.4	218.8	227.7	221.7	240.7	252.6	247.1	2 2	\ a	* *
8466	63	8.	9.		ກເ	đ٠	254.4	-		7.//2			. 7	0.830
8467	153.5	60 P	198.4	215.5	212.5	• *	240.B *			**	;*		•	;
0468 0440	24.	6 a	, E		242 3		251.2		59.	-69	71	69	67.	72.
8407 8478	. 4		. 06	199.3	215.2	218.5	227.7	229.4	235.1	241.1	247.2	251.9	254.3	250.7
8471	5	7.	35	•	230.5	~	245.7	Š.	60.	19	99	7	•	63.
8472	62.	83.	04.	-	225.9	_	255.5	١,	3	96	98	2	94.	02.
8473	56.	69	*	*	*		*	*	*				*	* ,
8474	60.	74.	01.	-	•	228.1	229.4	242.5	252.7	248.6	260.5	266.9	263.7	264.1
8475	62.		207.0	218.1	231.2	237.6	249.4		58.	52	9	7 5	9 4	10
8476	65.	85.	07.	ÇN.	_	246.2	255.2	98	9	₹	;	7 8	. 4	
8477 .	64.	80.	11.	P)	m	260.7	255.5	67.	4.	7	``	g.	. *	. *
9479	57.	73.	*				*	* (• ;	•	• [·		, G
8479	51.	67.	82	194.7	198.8	208.0	218.7	219.6	221.8	255.7	B . / 7.7	225.1	222.2	7.07.0
8480	58.	65.		_	, b, 1	82		9 1		6 6	0		, ,	, ×
8481	55.	35.	96.	_	s.	35.	4	55.	2.	,	9	Ċ	•	÷
GROUP	4 FEM	EMALES -	800.000	OO MG/KG										
20	53	35	W.	16.	4	κ.	- N	48.	ு	58.	69.	65.	68.	283.6
50	56.	3	69	07.	0	4	ĸ.	240.3	244.2	243.6	252.2	254.2	253.1	20
20.			186.4	m	214.4	٠	233.2	36.	237.2	42.	41.	57.	48.	45
50	56.	65.	*	*	*	-	*	*		•	*	*	•	* !
50	62	85.	ς.	03.	220.5	25.	230.0	224.9	vo		46.	43		ر د ا
5	68.	87.	-	27.	243.6	52.	260.0	254.4	O 1		9			
20	56.	9	œ.	07.	221.2	27	223.7	234.5	~ *		4 4	4 4 4 4		
20	63	. 99	┇,	9	218.7	4.5	223.5	219.0	^ 0		. u.c			, 5
5	53.		176.5	181.8	198.B	204.8	196.7	212.1	270 0	945 7	257.2	257.3	261.9	256.5
2 1		?	٠,		2.712		0.000	271.5	∙ •		8	8		78
2 2		N 4	• u	. 5	207.1		227.6	232.7	, vo		45.	49		55
7 5	: -	, ,	٠.	. 6	211.6	27.	236.2	235.9	- CO		54.	65.	*	*
	99	7	*	*	*	*	*	*		*	*	*	*	•
51		7	05.	20.	m	39.	46.	54	48.	.99	. 69	37.	68.	_
51	54.	66.	75.	90	B	13.	17.	25	19.	29.	38.	53.	32.	
5	55.	76.	91.	90	8	17.	24.	232.4	242.2	239.9	245.2	265.7	255.0	259.4
8519	172.0	197.9	210.9	225.9	223.7	248.3	251.9	258.2	55,	57	61.	<u>,</u>	` *	
22	42.	60.	33	80.	r a			9	6	7 130		259 1	6 676	971.9
22	. 99	91.	ů.	7.	\	``	ζ.	248.2	•	7.		2	9	:

- 100 -

APPENDIX 4

Individual Food Consumption

2008A/ID:178-33

ANIMA							WEEKS	,	c	•	;	13	11	
NEBER	1	2	3	4	2	9	7	20	<u>,</u>	9	-	1	***	
GROUP	1 MALES	1	CONTROL											
				4	*	100		ž	%	7.	ξ.	31.	*	
8362	, <u>5</u>	D U	1/1.0	֡֞֞֞֓֓֞֜֝֓֓֓֓֓֞֝֓֓֓֡֟֝	*	١ ي		50	50.	5.	40.	43.	*	
	1/4.2	167.7	٠.	178.6	*	180.0	167.1	172.5	168.6	179.7	172.3	170.9	*	
0 1	104 0	t v		7	*	5		82	6.	ő	92.	6	* :	
63720	149 0			. 2	*	4		52	4.	Š.	6.	25	* :	
9700	157.7		191	90	*	2		2	68,	ž.	61.	91	* :	
470	101.00			2	*	2		3	69	Š.	60.	52.	* :	
8708	,,,,,			. 6	*	5		20	74.	4.	54.	51.	* :	
8569	1.4.	147.0	168 0	1	*	31		4	41.	ř.	35.	30.	*	
8578	104.1			; ;	* #	5		2	55.	50.	ξ.	62.	*	
877	D .				142.9	. 10		3	55.	58.	54	52.	40.	
8272	٠,			* 15	192.7			8	87.	7.	93.	95.	ž.	
8373	٠		2 0	֓֞֜֜֜֜֜֜֜֜֓֓֓֜֜֜֜֜֜֜֜֓֓֓֓֓֜֜֜֜֜֡֓֜֜֜֜֓֓֓֡֓֜֜֡֡֡֡֡֡	180 1	: =		2	7	7	69	61.	161.3	
85/4	G			: 1	141.0	<u> </u>		5	58.	96	57.	44	9	
8375	164.0	9 6			191	, K		- 69	76.	69	74.	63.	58.	
8376	9		į (141.0	, 7		2	74.	6.			76.	
8377	1/4.9			י פ	7.701				54	55.	57.		42.	
8378	•	7 :	8	òi	101	5 3		. [72	51.	53.		47.	
8379	178.9	7	96	5 6	7.76.	9 0		: 2	6	4	176.8		3.	
8380	•	•	₽	ò	1/4./	֓֞֜֝֜֜֝֓֜֜֝֓֜֜֜֜֓֓֓֓֜֜֜֓֓֓֓֓֡֓֜֜֡֓֓֓֓֡֓֜֡֓֡֓֡֡֡֡֡֡֓֜֝		3 4			52		55.	
38	162.6	68.	167.4	3	158.8	2		ì	:					
GROUP	2 MALES	. 53	100.000	00 MG/KG										
						;	,	1	*	*	*	*	*	
8402	45	*		*				ď		159 7	159.B	5	*	
8403	7	179.4	2	162.7	¢ :				1 7	143 1	156.9	5	*	
8404	91	183.8	192.3	160.4	* :	166.5	1/1.9	0.001	107.0	159 9	171.2	171.8	*	
8405	2	173.3	9	165.0	*			ָ ק	ì	121.4	173 3	5	*	
8406	8	89	8	179.7	*			ι	1 (0 0 7 1	7 691	. 2	* *	
8407	65	160.6	6	159.9	*		¥ į	•	, ,	1.77.1	147.3		*	
8408	166.2	173.4	9	199.6	* :		4 n	9 9		157.5	152.4	5	*	
8409	168.7	170.7	9	165.3	¥ :		,	7 F	' '	156.3	167.1	68	* *	
8410	180.1	183.4	2	1/9.9			0 0	`	; =	178.5	178.0	99	*	
8411	210.7	2	,	167.5	k 3		, ,	,	7	161.9	164.6	62	* *	
8412	176.0	8	, D	1/0./	֓֞֝֜֝֜֝֜֝֜֝֜֝֟֜֜֝֝֟֜֝֝֟֝֓֓֓֓֓֓֓֓֓֓֓֓֓֓֓֡֝֡֓֓֡֝֡		† f) [167.7	168.4	3	58	
8413	164.3	156.0	3	16/.1	15/.5		127.4	, ,	158.3	161.0	162.7	- 39	155.2	
8414	8	92	1/9.8	1/2.4	6		5 6	•	; ;	169 9	*	6	3	
8415	69	*	171.8	167.4	26.		₽	: 1	; *	**	*	;		
8416	5	211.2	*	200.7	*	* :	k)	: 1	: 1	*	*	*	*	
8417	65	163.3	*	*	*	*			• -	٠,	7	, R	5	
8418	68	184.5	170.2	75.	33	72.	3		;		ב ב	. 9	40.2	
8419	\sim		173.6	165.6	161.5	154.3	152.6	15/.0	161.5	100.7	170.2	152.7	132.6	
8420	160.4	61	158.6	51.	49.	39.	2	4.	ķ. ;	7 2	} ;	, ,	4 15	
B421	Ž	29	5		48.	Ö.	38	44.	45.	Š	4	\$		
ř	,													

* = DEAD ANIMAL ** = INVALID VALUE - FOOD WASTED OR SPILLED

														•							-																			
<u>, , , , , , , , , , , , , , , , , , , </u>		1	: :	*	*	*	*	*	*	*	*	*	*	*	* ;	144.2	1 }	. 95	169.1	51.			*	* : * :	* *	*	*	*	*	*	*	*	;	7 (` "	, ,	?∶	2.1.2) (8
13		7	•		96	*	123.6	*	138.8	*	ď.	125.3	ĸ.	* ,	164.9	70.	•	66	153.1	52.			170.1	174.7	124.9	175.8	163.0	2.96	141.1	153.4	* !	155.0	* 0	, , ,	; ; ;			164 6		4 6
11		144.2	*	155.8	*	*	132.9	*	138.4	*	157.6	37.	# : #	* L	, ,	· ·	*	149.5	*	152.2		,	1/6.1	181.2	145.8	181.4	173.7	139.0	133.5	150.6	* :	151.2						150.0		
10		. 64	158.9	•	150.9		140.1		143.6	*	62.	151.6	; ;	, ,	, <u>.</u>	÷œ	*	99	153.8	56		3	* [147.6 0.741	130.3	177.4	155.5	143.6	135.9	149.6	* F	15/.5	* 171	` .	* *	*	* *	45	0 671	ŏ
6		40.	49	159.2	57.	*	129.5	*	136.3	* (•	156.1		r R	150.1	200	*	57.	151.3	55.		ŗ	94		139.7	54.	ĸ	64.	:		ū	7.1.61	- 73	,			N LC	139.2	×	0
6		44	52.	154.9	55.	*	160.9	* !	155.1		٠, ,	127.9	1 * *	v	153.5	: 19	!	4	162.2	61			֓֞֓֞֓֞֓֞֓֜֓֓֓֓֓֓֓֓֓֓֡֝֓֓֓֡֝֡֓֓֡֓֡֓֜֝֓֡֓֡֝֡֓֡֓֡֡֝֡֡֓֡֝	152.1	142.2	*	149.3	9		4 	1 20 %	•	4	. 2	178.3	•	*	168.4	161.9	ö
		41.	56.	149.2	63.	*	163.4	* (-	7 2	•	•	*	55	158.5	58.	*	50.	163.9	E		5		160.3	41.	* *	* * (, d		121 8	1 k	. * [41.	19	171.8	60.	*	161.2	60.	;
9			2	155.5	9	ì	176.1		127.8	151	147 6	147.7	*	147.8	161.8	56.	*	64.	167.4	70		~	1	. 16	149.9	8	2	2 [, ,	١,	<u> </u>	•	65	32.	80.	67.	55.	161.7	62.	
2		•	•	*	*	•	•			* *	*	*		158.	166	163.	*	164.	167.4			*	*	*	* *	* : * :	* *	* *	*	*	160.5	*	48	50	7	69	46	157.8	26	
4	00 MG/KG	138.3	146.6	164.7	152.2	* 0	15.0.8	141.0	159 7	156.5	158.8	186.1		157.7	167.5	175.0	* (198.9	154 1	1.001	O MG/KG	181.9	160.0	186.0	143.7		, e	. =	. 95	162.1	25	*	148.9	144.6	* * * .	171.4	167.7	166.6	160.3	
2	200.000	158.5	8	7.9.7	0		7 7	7,7	2	157.8	61.		*		174.7	-	* !	٠.	173.5	`	800.000	-	165.3	99.	157.8		. 6		48	53	.99	*	4.	47	65	Ž.	161.5	54	ž.	L
2	ES .	167.9	1/2.2	101	101.4	179 1	162.1	157.5	182.3	157.8	162.8	198.3	192.5	68	172.8	• 1	• 'i	Ġŗ	174.2	:	ı		8	145.1	157.1	151.7	138.8	50	9	62	167.9	61	67	39	; 9	5.	49	, 52	101.4	ì
4	3 MALES	93	٠.	, 4	5 2					161.1			90.	60.	R	ζ.	* ′	; =	173.6	,	4 MALE	66	4		9 7		152.B	157.8	154.2	157.3	171.8	169.5	138.8	117.4	0.8.1	161.0	į;	⊒•	1.601	0,
NUMBER	GROUP	8442	0440	8445	8446	8447	8448	8449	8450	8451	8452	8453	8454	τ, τ	6456	t A	5.5	6,4	· •		GROUP	8482	4	6 6	8487 8484	68	6	æ	\$	8491	<u>.</u>	<u>.</u>	<u>S</u> 9	<u> </u>	<u> </u>	<u> </u>	<u> </u>	2 5		122

^{* =} DEAD ANIMAL ** = INVALID VALUE - FOOD WASTED OR SPILLED

13		* 1			* *	*	* *	*	*	*	25	56	110.7	25	6	11	0	21	97.5	113.0		*		* *	*	* *	*	*	*	*	*	*		99.	22.	32	92.	103.9	24.	31.	02.
12		109.6	2 111	1.271	1.09.5	; =	112.1	35	118.0	87.7	18	2	112.2	3	=	109.1	133.2	123.5	108.9	117.3		106.7	119.4	137.4	114.3	107.0	116.1	137.6	139.8	99.1	92.5	*	11.	02.	13.	34.	10.	118.1	39.	36.	-
=		* ;	114.5	: :	136.0	114 4		16	110.6	35	26	2	Ξ.	6	7	6	-	9	* *	111.8		90	25	34	26	16	23	135.4	23	11	11	*	7	106.9	30	*		109.2			
10		118.7	, , , , , , , , , , , , , , , , , , ,	# # P	122.0			41		27.	65.	26.	30.	29.	16.	95.	18.	26.	*	118.6		113.5	118.2	129.2	131.8	112.5	119.3	127.7	131.7	124.0	115.2	136.1	115.2	102.9	127.5	130.0	111.1	107.4	130.6	137.5	124.3
6		117.7	26.		122.6			52		41.	43.	27.	82.		17.		29.	23		11.		10.	19.	43.		12.	35.	28	47		11.	*	14	11	58	143.3	9	108.8	129.2	138.5	121.5
60		111.0	•		126.6		119.2	133.0	125.1	135.3	142.5	121.0	110.6	76.2	*	109.5	*	*	*	119.9		13	25	35	126.6	16	3.0	144.6	8	20	9	*	8.	10.	21.	34.	19.	106.4	29.	30.	Ξ.
WEEKS		118.6	119.0	158.0	122.4	7.1/1	126.1	150.1	126.9	140.8	121.9	122.9	110.1	121.0	120.1	*	111.4	126.3	104.4	IC.		15.	23.	_	30.		31.	150.0	29.	17.	60	26.	Ξ.	80	15,	25.	19.	07.	27.	*	127.6
9		125.7	* (ч.	155.4	• •		٠ax	0.	. 40	(A)	vo	a	\sim	0	•	m	_	. N	_		116.1	129.4	167.3	140.1	132.4	135.3	154.1	119.8	127.8	120.8	127.3	118.1	106.1	123.4	*	122.9	122.9	136.4	147.2	122.7
7.		*	*	* :	* 1	: 4	* *	*	*	*	.5	2	110.1	5	Ξ	3	5	26	2	117.7		*	*	*	*	*	*	*	*	*	* *	vo	m	TC.	m	M	٧.	115.2	\mathbf{r}	- 90	TC.
4		114.1	22.	42.	121.2	;;	ġg	:	. 6	29	54	22	2	99	5	*	96		*	119.2	38 MG/KG	121.4	126.2	137.0	124.6	119.2	137.8	138.4	139.8	107.1	121.7	125.0	119.1	104.8	114.8	153.0	117.0	125.0	127.7	132.0	130.9
3	CONTROL		29.	4	29.			;;	141.8	32.	. 7	28.	7	23.	Υ.	*	121.4	44	*	127.8	100.000		46,	47	*	148.3	143.7	153.6	152.7		132.1	*		Κ.	27.	.09	27.	36	41.	20.	43.
2	FEMALES - I	1.	26.	•	145.6	77	•	} !		•	53		20.		28.		36.	41		132.5	FEMALES	120.6	*		1	33	53.	36.	÷	28.	è.	27.	32.	8	24.	51.	33.	29	38.	ö	133.1
-	1 FEM		19.	33	143.8				, 0	4.4	56	126.3	25.		25		26.		10.	128.3	2 FEM	124.1	143.8	32	. *	144.8	7	38.		37.		71.		17.	22.	46.	13	27.	48	49	45
AN 1 MAL NUMBER	GROUP	38	38	38	8385	200	38		00	\ D		, B	. 6	3	39	8397	. 6	ç	, 4	8401	GROUP	8422	42	42	5	8426	42	8428	8429	5	8431	5	5	8434	W	5	5	. 5	8439	4	4

^{** *} INVALID VALUE - FOOD WASTED OR SPILLED

HLA 2399108

ANTMAL		2	,	4	5	9	WEEKS 7	6	٥	10	17	12	13	
GROUP	3 FEM	FEMALES -	200.0000	OO MG/KG										
9462	154.2		147.7	133.3	*		128.3	125.8	10.	40		113.0	*	
£ ;		96		103.9	*	99.5	3	101.2	9.86	266	96.8	96.2	*	
404		. :		129.0	* :		120.9	109.7	┰.	vo	115.6	114.7	*	
å ;		164.9	9,	* !	* :	•	• ;	177.7		∓ `	*	187.9	*	
9 \		٠ <u>۱</u>		147.6	* :	135.6	133.4	139.5	147.8	134.7	131.9	134.2	*	
, o 7 6 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7		7 0	, a.	125.5			* :	128.9	4	* :	105.7	118.3	* : *	
400		117.2	. ,		k 1	Š	č	* 0	ċ		# ! !	ļ	* :	
404 607		7 6	ė :	122.1	* *	, C	7	1.66	21		93.2	5	* :	
9/4 1		128.8	4 1	711	* :	3	2	104.4	9	•	103.8	6	*	
1,5		٠.	155.2	146.9	# 1 # 1	141.9	137.5	130.8	142.2	130.1	129.1	123.8	*	
7/5		151.0		116.7	* :	~	35	122.3	62	_	119.7	23	*	
6/4		• ,		•	* 1	,	i	*			*	*		
4/4		24	* * !	108.0	118.5	146.9	130.5	131.0	127.1	134.2	114.3	113.6	120.4	
, t			?!	N	125.2	9	5	127.8	•	┗	126.9	127.5	*	
9/6		132.6	133.9	N.	131.9	<u> </u>	12	116.5	119.0	ш-	124.B	117.7	118.7	
) () (157.9	46,	4,	142.9	130.6	118.6	_	121.5	106.7	113.7	102.5	115.8	ν,	
) (T		• (- 4	•			*			*	*		
6/4	*	149.8	*	9	96	109.1	107.1	102.0	101.4	100.4	8	8	6.86	
	175.1	4. 18.	141.8	134.6	LC 4	5	<i>.</i>	27.	37.	36	0	4	0	•
181	31.	37.	35.	128.2	30	2	27.	22.	٠.	2	23	26	23	
GROUP	4 FEMAL	LES -	000.000	O MG/KG										
8502	142.6	131.2	151.3	100	*	164.8	*	48.	29.		*	10	*	
503	_	120.9	32.	4	*	126.6	07.	106.8	110.4	*	112.9	9	*	
04		17	*	2	*	125.3	108.6	*	*	*	*	108.5	*	
.05		*	*		*	*	*	*	*	*	*	*	*	
90:		35.	139.4	135.5	*	117.7	TU.	137.3	E.	123.3	*	141.6	*	
.07			55.	22	*	135.1	0	130.3	7	33	145.6	130.4	*	
80		128.1	22.	*	*	93.4	120.9	108.3		02	119.8	105.2	* *	
606			28.	113.4	*	101.7	\sim	107.1		1	16	119.3	*	
510		03.		*	*	9.68	ъ.	97.3		99	111.9	103.9	*	
511		41.	28.	128.9	*	117.1	•	124.9		01	22	109.6	*	
512		131.3	148.7	*	*	158.9	*	*	135.8	148.8	86	128.6	*	
513		•		135.5	41.	129.8	133.9	132.8		13	124.2	119.1	116.9	
1514		135.6	36.	3	177.4	163.3	*	136.6	138.8	38	180.1	*	*	
i1 5		*	*	*	*	*	*	*		*	*	*	*	
516		187.0	*	*	*	165.8	*	*	~	32.	31	_	165.8	
17		124.0	40.	31.	35.	*	*		₽	21.	23	v	121.6	
18	130.3	121.7	124.4	16.	15.	103.4	125.1	123.1	169.3	114.1	113.4	124.6	115.9	
19	139.9	140.1	*	129.9	137.3	121.4	-	112.0	114.8	05.	14	_	114.0	
20	116.1	109.6	m	27.	23.	107.0		-		*				
521		136.4	œ		35.	121.2	129.0	121.3	115.7	120.9	114.7	121.6	125.6	

^{* *} DEAD ANIMAL ** = INVALID VALUE - FOOD WASTED OR SPILLED

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APPENDIX 5

Individual Ophthalmoscopic Findings



2399-108

APPENDIX 5 INDIVIDUAL OPHTHALMOSCOPIC FINDINGS

Animal Number	Group	<u>Sex</u>	<u>Interval</u>	<u>Finding</u>
8404	2	M	Pretest	Left eye - Small hyaloid remnants with small vitreal hemorrhages (judged by ophthalmologist to be a common developmental finding which would not affect test results).
8418	2	M	Pretest	Left eye - Small hyaloid remnants with small vitreal hemorrhages (judged by ophthalmologist to be a common developmental finding which would not affect test results).
8373	. 1	M	Terminal	Right eye - focal zone of retinal degeneration
8452	3	M	Terminal	Right eye - generalized retinal degeneration. Left eye - early diffuse retinal degeneration.



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202/363-7303

April 1, 1986

Gary W. Wolfe, Ph.D. 1330 -B Piccard Drive Rockville, MD 20850

Subject: Ophthalmoscopic Examination of 240 Rats, Study 2399-108

March 27, 1986

All animals were found to have no visible lesions except the following; male # 86 and male # 110 - both had small hyaloid remenants with small vitreal hemorrhages in their left eyes. This is a commonly identified developmental abnormality. Its presence will not affect test outcome.

Nancy M. Bromberg, V.M.D.



Nancy M. Bromberg, V.M.D., M.S. Diplomate, American College of Veterinary Ophthalmologists 4105 Brandywine Street, Northwest Washington, D.C. 20016 202/363-7303

Jul 14, 1986

Pat Vanatta Hazleton Laboratories 1330-B Piccard Drive Rockville, MD

Subject: Ophthalmoscopic examination of 80 Rats, Project No. 2399-108 July 9, 1986

All animals examined were found to have no visible lesions except for the following:

Group I male #8373 Right eye focal zone of retinal degeneration. Group III Male # 8452 Right eye generalized retinal degeneration; left eye early diffuse retinal degeneration.

Due to the infrequency of abnormal ophthalmoscopic changes, I do not believe either of these findings to be dose-related.

Nadcy M. Bromberg, V.M.J., M.S.

Dip., AYC.V.O.

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APPENDIX 6

Individual Clinical Hematology Values



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KEY TO HEMATOLOGY

Leukocyte Differentials

Blast Cells	BLAST
Metamyelocytes	META
Band Neutrophils	BAND
Segmented Neutrophils	SEG
Lymphocytes	LYMPH
Monocytes	MONO
Eosinophils	EOSIN
Basophils	BASO

Cell Morphology

Echinocytes	ECHINO
Target Cells	TARGET
Hypochromic Cells	HYPO
Poikilocytes	POIK
Acanthocytes	ACANTH
Polychromatophilic Cells	POLY
Nucleated RBC'sa	NRBC
Howell-Jolly Bodies	HJBODY

Cell morphology findings are graded by the following method.

- = None Present

T = Trace Numbers Present

1 = Slight Numbers Present

2 = Moderate Numbers Present

3 = Marked Numbers Present

4 = Severe Numbers Present

aExpressed as a percentage of 100 WBC's counted.

APPENDIX 6
INDIVIDUAL CLINICAL HEMATOLOGY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS
WEEK -1 MALES

A RETIC MI/UL		.20	23	.21	.26
RETIC % RBC		6.0	4.1	5.1 4.0	4.7
PLATELET TH/UL	CNIT:	858 1076	1328	1277 1425	1193 226.4
HCT %	: DOSAGE	43.5	33.7	33.4 32.3	34.4 5.43
HGB G/DL	: BASELINE	16.0	14.5	15.3	14.9
RBC MI/UL	DOSE LEVEL:	6.74	7.75	5.20 5.20 5.23	5.48
	R				
AN I MAL NUMBER	GROUP:	08522	08523	08524 08525 08525	MEAN S.D.

APPENDIX 6
INDIVIDUAL CEINICAL HEMATOLOGY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS
WEEK -1 MALES

AN I MAL NUMBER	WBC	BLAST TH/UL(%)	META TH/UL(%)	BAND TH/UL(%)	SEG TH/UL(%)	LYMPH TH/UL(%)	MONO TH/UL(%)	EDSIN TH/UL(%)	BASO THYUL (%)
1 1 1 1 1	1 1 1 1	1 1 1 1 1 1		1 1 1 1	!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!	1	1		
GROUP: 5	DOSE LEV	LEVEL: BASELINE		DOSAGE UNIT:					
08522	10.1	.0(0)	ŏ.	(0)0.	1.3(13)		.3(3)	.10 1)	(0)0.
08523	11.1	(0)0.	ŏ.	(0)0.	.4(4)		.1(1)	.2(2)	0 00.
08524	16.2	(0)0.	(0)0.	(0)0.	1.1(7)	14.6(90)	.5(3)	(0)0.	(0)0.
08525	16.6	(0)0.	ĕ.	(0)0.	.7(4)		.7(4)	(0)0.	(0)0.
08526	11.9	(0)0.	0	.0(0)	(6)9.		.2(2)	.1(1)	(0)0'
MEAN	13.2	0.	0.	٥.	8.	11.9	4		0.
s.D.	3.01	00.	00.	00.	.37	2.94	.24	80.	00,

APPENDIX 6
INDIVIDUAL CÉINICAL HEMATOLOGY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS
WEEK -1 MALES

ANIMAL POLY TARGET ECHING NUMBER	NRBC	1 1 1 1 1 1	DOSAGE UNIT:	+		•	2	,
POLY TARGET	ECH1NO	1	DOSAGE	•	+		•	
1 24646		1 1 1 1 1 1	BASEL INE	4	4	4	4	4
1 04600		1 1 1 1 1	rever:	ı	1	ŧ	1	-
ANIMAL NUMBER GROUP: 5 08522 08523 08524 08524	PG	i		2+	;	÷	2+	÷
	ANIMAL NUMBER	1 1 1	GROUP: 5	08522	08523	08524	08525	96580

APPENDIX 6 INDIVIDUAL CLINICAL HEMATOLOGY VALUES SUBCHRONIC TOXICITY STUDY IN RATS WEEK 4 MALES

					-	
$\Sigma \square$	RBC MI/UL	HGB G /DL	도~	PLATELET TH/UL	RETIC * RBC	A RETIC MI/UL
! ! !	; ; ;	1 1 1 1 1			1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	1 ! ! ! ! ! ! ! ! ! ! ! ! ! ! ! ! ! ! !
GROUP: 1	DOSE LEVEL:	r: 0	D05AG	DOSAGE UNIT: MG/KG	⁄KG	
08362	7.83	16.1	43.5	1479	1.7	.13
08363	7.93	15.2	43.8	1207	1.8	14
08364	7.48	15.1	42.2	1513	1.3	10
08365	7.90	15.4	46.4	1117	1.6	.13
99280	8.68	16.7	51.1	115	2.7	.23
08367	8.54	16.6	48.2	1211	۳.	.03
08368	7.48	14.9	43.0	1178	۲.	. 05
08369	7.34	14.6	40.3	1271	1.0	.07
08370	6.54	15.8	38.2	930	1.0	.07
08371	6.85	16.1	41.4	686	1.1	80.
MEAN	7.66	15.6	43.8	1101	1.3	10
s.0.	.671	.72	3.83	392.3		.058
GROUP: 2	DOSE LEVEL:	L: 100	DOSAG	DOSAGE UNIT: MG/KG	ЖĞ	
08403	7.89	15.5	47.1	971	1.5	.12
08404	7.83	15.6	46.3	1379	2.8	.22
08405	7.98	15.4	44.8	1206	Φ.	90.
08406	7.43	15.2	42.3	1298		.13
08407	7.19	15.7	44.5	1158	2.4	.17
08408	9.08	15.8	46.3	1199	٥.	20.
08409	9.26	15.2	46.5	1082	1.6	.13
08410	•	15.6	45.1	1297	1.5	.12
08411	6.51	15.0	38.8	1072	1.7	.11
08412	7.73	15.8	42.1	1437	1.6	.12
MEAN	7.66	15.5	44.4	1209	1.6	1.2
S.D.	.507	22	2.60	145 0		77.
	;	į	,) - -		7 7 7

APPENDIX 6
INDIVIDUAL CÉINICAL HEMATOLOGY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS
WEEK 4 MALES

A RETIC MI/UL		. 02	.12	90.	60.	.11	.10	.13	90.	.07	.07	.08		.035		.11	.10	.11	.12	90.	.11	.12	.10	.11	60.	.10	.018
RETIC % RBC	9	5.	1.5	۲.	1.1	1.5	1.2	1.7	α .	6.	٥.	1.0	į	.45	9	1.5	1.3	1.4	1.6	٥.	1.5	1.7	1.2	1.5	1.2	1.4	.23
PLATELET TH/UL	DOSAGE UNIT: MG/KG	1150	1272	1433	1387	1210	1075	1276	1333	1122	1153	1241	1 1	119.0	UNIT: MG/KG	1111	1159	1221	1076	1194	1147	1395	NO TEST	1226	1213	1194	91.4
五子 *	DOSAGE	43.7	43.8	45.7	45.2	42.6	46.8	43.8	46.0	46.4	41.3	44.5		1.78	DOSAGE	42.6	41.8	47.0	42.1	40.3	44.2	40.3	•	41.1	40.3	42.7	2.68
HGB G/DL	: 200	15.4	15.3	16.2	16.3	15.2	15.3	14.5	15.8	16.1	15.2	ر بر		.56	900	15.5	15.4	15.9	15.1	15.6	15.8	14.4	17.0	16.0	15.8	15.6	. 67
RBC MI/UL	DOSE LEVEL:	7 66	7.B1	. B.	B. 04	7.29	8.36	7.75	7.91	7. B6	7.62	7 83	\ o . \	.288	DOSE LEVEL:	7.42	7.46	8.19	7.40	96.9	7.62	7.27	8.60	7.20	7.18	7 53	497
ANIMAL NUMBER	GROUP: 3	08770	08441	48860	00444 08445	18447	08448	08449	08450	08451	08452	40	Z	S.D.	GROUP: 4	08482	08483	08484	08485	08486	08487	08488	08489	08490	08491	100	S.D.

APPENDIX 6
INDIVIDUAL CEINICAL HEMATOLOGY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS
WEEK 4 MALES

				* (1)					
ANIMAL NUMBER	WBC TH/UL	BLAST TH/UL(%)	META TH/UL(%)	BAND TH/UL(%)	SEG TH/UL(%)	LYMPH TH/UL(%)	MONO TH/UL(%)	EOSIN TH/UL(%)	BASO TH/UL(%)
! ! !	!	1	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1		† † † † †	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1		1	1 1 1 1 1 1 1
GROUP: 1	DOSE LEV	LEVEL: 0	DOSAG	DOSAGE UNIT: MG/KG	/KG				
08362	•		.0 0	(0)0.	1.8(12)	12.9(86)	.3(2)	(0)0.	(0)0.
08363	10.2		(0)0.	(0)0.	.5(5)	9.7(95)			
08364	•				3.4(16)	17,6(82)	(0)0'		
08365	17.3	(0)0.		0 00.	1.9(11)	15.4(89)	(0)O.		
08366	12.9				7.4(57)	5.5(43)			
08367	13.4	(0)0.	(0)0.		(9)8.	12.5(93)			
89280	17.1				2.6(15)	13.9(81)			
69£80	16.3				2.3(14)	13.9(85)			
08370	19.8		(0)0.	0000	2.2(11)	17,6(89)			
08371	19.3		(0)0.		2.7(14)	16.4(85)	.2(1)	(0)0.	(0)0.
MEAN	16.3	6	=	-	7 6		-	+	c
0	07 2						.	٦.	-
	7.4B	.	a .	90.	1.91	3.74	.13	-	00.
GROUP: 2	DOSE LEVI	LEVEL: 100	DOSAGE	DOSAGE UNIT: MG/KG	'KG				
08403	9.8	(0)0.	(0)0.	.1(1)	1,1(11)	8.5(87)	(0) 00.	.16.13	0.0
08404	11.7	(0)0.	(0)0.		2.8(24)	8.4(72)	.1(1)		
08405	٠		(0)0.		1.8(13)	12.2(87)			
08406	13.5			(0) (0)	.7(5)	12.3(91)			0.00
08407					2.7(17)	12.7(81)			
09408	-	(0)0.	(0)0.		1.5(8)	17.1(90)			
08409					1.1(6)	16.5(93)			
08410	12.4				2.0(16)	9.7(78)			
08411	19.6	(0)0.			3.5(18)	15.5(29)			
08412	19.2		.0(0)	(0)0.	1.7(9)	17.3(90)	2(1)	0000	(0)0.
MEAN	15.3	۰.	0.	0.	1.9	13.0		.2	
S.D.	3.49	00.	90.	.03	.88	3.45	=	.20	00
									,

APPENDIX 6
INDIVIDUAL CLINICAL HEMATOLOGY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS
WEEK 4 MALES

ANIMAL	WBC TH/UL	BLAST TH/UL(%)	META TH/UL(%)	BAND TH/UL(%)	SEG TH/UL(%)	LYMPH TH/UL(%)	MONO TH/UL(%)	EOSIN TH/UL(%)	BASO TH/UL(%)	
GROUP: 3	DOSE LEV	EVEL: 200	DOSAG	DOSAGE UNIT: MG/KG	⁄KG					
08442	9.8	(0)8.	(0)0.	(0)0.	1.2(14)	7.1(83)	.0 O.	.3(3)		
08443	11.7			(0)0.	1.5(13)	10.1(86)	(0)0.	(1)(1)	(0)0.	
08444	16.4				3.1(19)	12.6(77)				
08445	19.4	(O)O.	0 0.	(0)0.	3.1(16)	15.9(82)	00.00	.4(2)		
08447	26.2				4.2(16)	21.5(82)				
08448	21.1				1.3(6)	19.0(90)				
08449	16.9				4.7(28)	11,7(69)				
08450	22.5				2.9(13)	19.6(82)				
08451	18.0				3.8(21)	13.9(77)				
08452	23.2		.0 .0.	(0)0.	.5(2)	22.5(97)	.2(1)		(0)0.	
MEAN	18.4	9	0.	0.	5.6	15.4	.2	7.	0.	
S.D.	5.34	00.	00.	00.	1.42	5.16	.20	. 19	00.	
GROUP: 4	DOSE LEVEL:	EL: 800	DOSAGE	E UNIT: MG/KG	/KG					
08482	11.8	(0)0'	(0)0.	(0)0.	2.8(24)	8.6(73)	.2(2)	.1(1)	.0 0	
08483	15.7	(0)0.	(0)0.	.2(1)	.8(5)	14.4(92)	.2(1)	.2(1)		
08484	14.3		(0)0.		3.4(24)	10.7(75)				
08485	18.1	(0)0.			1.6(9)	16.3(90)	(0)0.	.2(1)	(0)0.	
08486	12.2	(0)0.		(0)0.	1.8(15)	10.2(84)				
08487	23.7			(0)0.	3.3(14)	19.4(82)				
08488	24.0	0000	(0)0.		6.2(26)	17.3(72)	.5(2)			
08489	20.6			(0)0.	1.6(8)	18.3(89)		(6 3)		
08490	14.3	(0)0.	(0)0.	(0)0.	1.3(9)	12.6(88)			٠.	
08491	18.0	(0)0'	.000.	(0)0.	2.2(12)	15,1(84)	.2(1)	.5(3)	(0)0.	
MERN	17.3	ė	0,	0	2,5	14.3	۲.	٣.	0.	
S.D.	4.41	00.	00.	90.	1.55	3.66	.19	.22	00.	

APPENDIX 6
INDIVIDUAL CLINICAL HENATOLOGY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS
WEEK 4 MALES

ANIMAL NUMBER	POLY	TARGET	ECHINO	ACANTH	НЭВОДУ	POIK	NRBC
	 	1 1 1 1 1 1 1 1	1 1 1 1	 	1 1 1 1 1	 	1 1 1 1 1 1 1
GROUP: 1	DOSE LEVEL:	JEL: 0	DOSAG	DOSAGE UNIT: MG/KG	,×G		
08362	-	•	*	-			
08363	_		5+		,	1	1
08364	 - -	t	4	•	ı	•	,
08365	1:	-	*	1		,	·
99280	_		*		•	ı	,
08367	_	1	*	1	•	:	,
89680	_	•	2+	_		•	,
08369	}	1	4	ļ	•	1:	1
08370	-	1	+ 4	t	1	1	
08371	-	1	*	1	1	1	1
GROUP: 2	DOSE LEVEL: 100	ÆL: 100	DOSAG	DOSAGE UNIT: MG/KG	'KG		
09403	:	,	2	ı	•	1	i
08404	1.	•	2+	•	,	1	
08405	-	:	÷	-	ı	•	
08406	-	-	• 4	t	ı	1	. 1
08407	_	-	4			1	1
08408	-	,	2+		,	ı	1
08409	-	1	2+	•		1	•
08410	_	•	2+	ı	•	1	1
08411	-		4	_	ı	ť	
08412	-	1	*	ı	1		1
GROUP: 3	DOSE LEVEL:	EL: 200	DOSAGE	DOSAGE UNIT: MG/KG	'KG		
08442	-	ı	*	•	1	ı	1
08443	-	1	4	 	1	1	,
08444	-	1+	3+	. ,		•	
08445	-	1	4	•	ı	1	,
08447	_	+-	4+	•	1	1	,
08448	_	1	+1	•	•	-	ı
08449	-	•	2+	_	1	•	ı
08450	-	1	*	1	1	_	ı
08451	-		3+	1	1		ı
08452	_	•	44		1		1

APPENDIX 6	INDIVIDUAL CCINICAL HEMATOLOGY VALUES	SUBCHRONIC TOXICITY STUDY IN RATS	LIFFK A MALES
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NRBC	1		ı	1	•	•	•	•	•	t		ı
POIK	1			1	1	1		1	ı	1	•	1
нэвару	1	/KG		1	1	•	1	•		1	•	
ACANTH	1	DOSAGE UNIT: MG/KG	i		,					•	•	1
ECH1N0		DOSAGE	3+	44	3+	4.	++	2+	2+	3+	• 4	4
TARGET	† 	DOSE LEVEL: 800	1	-	+	•	_	1	ı	,	1	,
POLY	1	DOSE LE	-	-	_	_	_	-	-	-	-	-
ANIMAL	NOTIBER	GROUP: 4	08482	08483	08484	08485	08486	08487	08488	08489	08490	08491

APPENDIX 6
INDIVIDUAL CLINICAL HEMATOLOGY VALUES
SUBCHRONIC'TOXICITY STUDY IN RATS
WEEK 13 MALES

ANIMAL NUMBER	RBC M1×UL	HGB G/DL	HCT *	PLATELET TH/UL	RETIC * RBC	A RETIC MI/UL
GROUP: 1	DOSE LEVEL:	i. 0	DOSAG	DOSAGE UNIT: MG∕KG	'KG	
08362	8.31	15.4	41.9	1272	1.5	.12
08364	6.83 0.83	16.0 15.1	44.2	1138		.10
08365	8.60	15.8	43.9	1011		
08366	8.47	15.5	43.4	1327) Y
08367	8.35	15.5	42.8	1299	1.0	80.
89280	8.66	16.1	45.2	1198		90
08369	8.39	15.3	41.4	1392	1.1	60
08370	8.84	16.3	45.4	966	r.	.04
08371	9.00	15.8	44.0	793	۲.	90.
MEAN	8.47	15.7	43.4	1181	٥.	.08
s.o.	.262	.38	1.41	195.9	.30	.024
GROUP: 2	DOSE LEVEL:	L: 100	DOSAGE	UNIT: MG/KG	KG	-
08403	8.77	16.7	46.8	1033	9	70.
08404	8.42	15.9	43.7	1254	2.5	.21
08405	7.78	13.9	38.8	1351	1.3	.10
08406	8.74	16.1	44.7	1087	1.6	.14
08407	80.8	16.0	45.8	1069		. 19
08408	8.53	15.6	43.8	1040	.2	. 02
08409	8.84	15.5	43.8	696	1.0	60.
08410	8.39	15.8	43.5	1032	. 1.1	.00
08411	•	16.2	45.0	1058	1.3	11,
08412	8.97	15.9	43.5	1239	9.	50.
MEAN	8.50	15.8	43.9	1113	1,3	11
s.o.	.362	.73	2.11	123.4	17.	. 059

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APPENDIX 6
INDIVIDUAL CLINICAL HEMATOLOGY VALUES
SUBCHRONIC.TOXICITY STUDY IN RATS
WEEK 13 MALES

NUMBER	MI/UL	70/9	*	TH/UL	* RBC	MI/UL
GROUP: 3	DOSE LEVEL: 200	:L: 200	DOSAG	DOSAGE UNIT: MG/KG	KG	
08442	8.77	16.4	45.6	1038	w. w.	.08
08444		16.0	44.6	1297	1.6	.14
08445	9.81	16.2	44.7	1362	2.0	.18
08447	8.07	15.1	42.1	1199	3.5	.28
08449	8.41	14.8	42.7	1137	.5	.04
08451	8.50	15.9	45.0	1069	Θ.	.07
08452	9.14	16.1	44.9	1006	.2	. 02
08453	7.93	14.7	41.2	1067	٥.	.07
18455	8.64	16.0	44.0	1257	۲.	90.
MEBN	8.59	15.7	44.0		1.5	.12
S.D.	.374		1.47	119.0	1.19	.101
GROUP: 4	DOSE LEVEL:	:T: 800	DOSAGE	E UNIT: MG/KG	KG	
08482	8.04	15.1	42.2	885	1.8	.14
08483	8.53	16.1	44.4	1070	1.3	.11
08484	8.89	15.7	45.1	1159	٠.	. 04
08485	8.49	15.6	43.5	1026	2.6	. 22
08486	8.57	16.0	44.7	1122	1.8	.15
08487	8.60	16.6	46.2	1139	1.6	.14
08488	6.45	11.6	32.7	1388	۲.	. 05
08489	9.48	17.0	47.8	1115	ĸ.	.03
08490	8.77	16.7	46.0	1076	œ.	.07
08492	9.24	17.1	46.7	1054	.3	.02
MEAN	9.51	15.7	43.9	1103	-	.10
_	700	1.59	4.26			. 065

APPENDIX 6
INDIVIDUAL CLINICAL HEMATOLOGY VALUES
SUBCHRONIC+TOXICITY STUDY IN RATS
WEEK 13 MALES

BASO TH/UL(%)		00.		n 0 .
EOSIN TH/UL(%)		.09	.00.00 .00.00 .00.00 .00.00 .00.00 .00.00	.12
MONO TH/UL(%)	10.4.2.0.0.0.0.0.0.0.0.0.0.0.0.0.0.0.0.0.	.13	0.0000000000000000000000000000000000000	à.
LYMPH TH/UL(%)	10.4(78) 10.8(96) 18.4(84) 15.7(92) 12.8(79) 12.9(77) 13.8(83) 10.8(85) 11.2(77)	13.6	13.6(91) 8.6(85) 12.4(62) 9.1(85) 10.3(75) 15.8(97) 11.7(96) 8.7(80) 15.3(75) 14.5(90)	5.72
SEG TH/UL(%)	2.7(20) .5(4) 2.8(13) 1.0(6) 3.4(21) 3.9(23) 2.8(17) 1.8(14) 3.5(22) 2.9(14)	2.5 1.10 ⁄KG	1.3(9) 1.4(14) 7.6(38) 1.6(15) 3.0(22) .5(3) 1.7(16) 4.7(23) 1.4(9)	7.73
BAND TH/UL(%) TH		.00 1 .00 1		nn.
META TH/UL(%) 1		.0 .00 DOSAGE		?
BLAST TH/UL(%)		.0 .00 EL: 100		a.
MBC TH/UL TH		16.3 3.36 DOSE LEVEL:	14.9 10.1 10.0 13.7 12.2 10.9 10.9 14.5	3.71
ANIMAL NUMBER		MEAN S.D. GROUP: 2	08403 08404 08405 08405 08400 08410 08411 08412	S.D.

APPENDIX 6
INDIVIDUAL CLINICAL HEMATOLOGY VALUES
SUBCHRONIC-TOXICITY STUDY IN RATS
WEEK 13 MALES

				WEEK 13	MALES				
ANIMAL NUMBER	WBC TH/UL	BLAST TH/UL(%)	META TH/UL(%)	BAND TH/UL(%)	SEG TH/UL(%)	LYMPH TH/UL(%)	MONO TH7UL(%)	EOSIN TH/UL(%)	BAS0 TH/UL(%)
GROUP: 3	DOSE LEVI	EVEL: 200	DOSAG	DOSAGE UNIT: MG/KG	УKG				
08447	13.5	.0(0)	(0) (0)	(0)0.	1,3(10)	11,6(86)			(0)0.
08443	15.6	(0)0'	0 0	(0)0.	1.4(9)	14.0(90)	(0)0'	.2(1)	(0)0'
08444	15.9				3.2(20)	12.6(79)			
08445	14.1		0 0.	0000	2.1(15)	11.7(83)			00 00.
08447	24.4				6.8(28)	17.3(71)			
08449	15.1	(0)0.			2.4(16)	12.5(83)			
08451	13.3				1.5(11)	11.7(88)			
08452	17.7				.7(4)	16.6(94)			
08453	19.5				3.9(20)	15.4(79)			
08455	23.6	(0)0.	(0)0.		4.0(12)	19.1(81)	(0)0.		
MEAN	17.3	0.	9	۰.	2.7	14.2	٦.	.2	0.
S.D.	4.02	00.	00.	00.	1.82	2.70	.11	.15	00.
GROUP: 4	DOSE LEW	EVEL: 800	DOSAGE	E UNIT: MG/KG	/KG				
08482	11.0	(0)0'	(0)0.	(0)0.	2.4(22)	8.4(76)	(0)0.	.2(2)	(0)0.
08483	15.2				(9)6.	14.1(93)			
08484	17.3	(0)0.	(0)0.	(0)0.	4.3(25)	12.6(73)	.2(1)	.2(1)	(0)0.
08485	22.9				2.3(10)	20.6(90)			
08486	9.6				1.2(13)	8.4(87)			
08487	18.0				2.9(16)	14.8(82)			
08488	20.5				5.3(26)	15.0(73)			
08489	21.9				1.3(6)	20.4(93)			
08490	12.3					11.1(90)			
08492	17.4		(0)0.	(0)0.	2.8(16)	14,4(83)	(0)0.		
MEAN	16.6	0.	٥.	0	2.4	14.0	٦.	.2	0.
S.D.	4.56	00.	00.	00.	1.48	4.21	.10	.16	.00

APPENDIX 6
INDIVIDUAL CLINICAL HEMATOLOGY VALUES
SUBCHRONIC-TOXICITY STUDY IN RATS
WEEK 13 MALES

ANIMAL NUMBER	POLY	TARGET	ECHINO	ACANTH	POIK
GROUP: 1	DOSE LEVEL	EL: 0	DOSAG	DOSAGE UNIT: MG/KG	Y.
08362 08363 08364 08365		1111		⊢ 1 ⊢ 1	
08366 08367 08368 08369 08370		11111	·	1 1	⊢ () ⊢ () (
GROUP: 2 08403 08404	DOSE LEVEL:	EL: 100 	DOSAGE - T	DOSAGE UNIT: MG/KG	. K
08405 08405 08407 08409 08410	•			. •	
U8411 08412 GROUP: 3	DOSE LEVEL:	- EL: 200	1 1+ DÖSAGE	- T DØSAGE UNIT: MG/KG	9
08442 08443 08444 08445 08447 08449 08451 08453					

APPENDIX 6
INDIVIDUAL CLINICAL HEMATOLOGY VALUES
SUBCHRONIC'TOXICITY STUDY IN RATS
WEEK 13 MALES

ANIMBER NUMBER GROUP: 4	POLY TARGE	TARGET	ECHINO DOSAGE	INO ACANTH DOSAGE UNIT: MG/KG	POIK
70700	- 1-	,	- 1-		'
00407	- 1	•	- 1		ı
J8484	_	•	_	1	
08485	_	ı	-	-	1
08486	-	•	_		1
08487	-	1	-	ı	1
08488	 	-	:	ı	
08489	 	1	-	ı	•
08490	-	,	ı		,
08492	-	1	_		i

APPENDIX 6
INDIVIOUAL CLINICAL HEMATOLOGY VALUES
SUBCHRONIC+TOXICITY STUDY IN RATS
WEEK -1 FEMALES

A RETIC MI/UL		. 25	. 15	. 25	.18	.23	.21
RETIC * RBC		4.9	4.2	5.3	3.8	5.0	4.6
PLATELET TH/UL	UNIT:	1227	1364	1430	1429	1311	1352 85.8
도 *	DOSAGE	32.7	23.2	29.4	29.0	28.8	28.6
HGB G/DL	BASEL INE	15.7	14.8	14.8	15.8	15.1	15.2 .48
RBC MI/UL	DOSE LEVEL: BASELINE	5.18	3.50	4.80	4.62	4.58	4.54
ANIMAL NUMBER	GROUP: 5	08527	08528	08529	08530	08531	MEAN S.D.

APPENDIX 6
INDIVIDUAL CLINICAL HEMATOLOGY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS
WEEK -1 FEMALES

ANIMAL NUMBER	WBC	BLAST TH/UL(%)	META TH/UL(%)	BAND TH/UL(%)	SEG TH/UL(%)	LYMPH TH/UL(%)	MONO TH/UL(%)	EDSIN TH/UL(%)	BASO TH/UL(%)
GROUP: 5	DOSE LEV	EVEL: BASELINE	NE DOSAGE	E UNIT:					
08527	18.2	(0)0.	(0)0.	(0)0.	(8) 3)		.5(3)	.2(1)	(0)0'
08528	17.9	(0)0'	(0)0.	(0)0.	1.4(8)	16.1(90)	.4(2)	(0)0.	(0)0.
08529	12.8	(0)0.	(0)0.	(0)0.	(9)8.		(0)0.	.1(1)	(0)0.
08530	14.4	0 00	(0)0.	(0)0.	1.7(12)		.4(3)	.1(1)	(0)0.
08531	13.6	.000	.0 .0	00 00	1.0(7)		.1(1)	.5(4)	(0)0'
MEAN S.D.	15.4	0.00.	00.	0.0.	1.1	13.8 2.48	.3	.2 .19	00.

APPENDIX 6
INDIVIDUAL CEINICAL HEMATOLOGY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS
WEEK -1 FEMALES

NRBC	DOSAGE UNIT:	1 1 1 1 1
ECHINO		* * * * *
TARGET	Z	4 4 4 4 4
	LEVEL:	H 1 1 1 1
POLY	DOSE	*
	r.	
ANIMAL NUMBER	GROUP: 5	08527 08528 08529 08530 08531

APPENDIX 6
INDIVIDUAL CCINICAL HEMATOLOGY VALUES
SUBCHROWIC TOXICITY STUDY IN RATS
WEEK 4 FEMALES

AN I MAL NUMBER	RBC MI/UL	HGB G/DL	#CT	PLATELET TH/UL	RETIC * RBC	A RETIC MI/UL
GROUP: 1	DOSE LEVEL:	r: 0	DOSAG	DOSAGE UNIT: MG∕KG	ЖG	
08382	5.88	14.8	34.1	1311	1.0	90.
08383	7.74	15.4	44.5	1311	1.1	60.
08384	7.37	15.3	42.7	1211	1.8	.13
08385	6.85	13.8	37.9	1182	1.3	60.
98280	69.9	15.7	37.4	1201	۲.	. 05
08387	7.76	15.4	43.7	1191	6.	.07
08388	8.00	15.5	45.8	1201	9.	. 05
08389	7.41	15.2	42.3	1102	1.3	.10
08390	6.50	14.5	37.4	1319	9.	.04
08391	6.34	15.0	35.2	1224	&	. 60
MEAN	2.05	15.1	40.1	1225	1.0	.07
5.0.	. 704	.57	4.16	.69	2 .38	. 029
GROUP: 2	DOSE LEVEL:	L: 100	DOSAG	DOSAGE UNIT: MG/KG	χe	
08422	6.63	14.6	38.7	1400	1.4	.09
08423	5.94	15.4	33.6	1320	1.9	.11
08424	7.68	16.0	45.0	1484	1.3	.10
08425	7.75	15.7	44.1	1415	2.2	.17
08426	6.40	15.9	37.6	1157	1.3	B0 ·
08427	6.71	15.5	39.3	1330	1.1	.07
08428	7.84	15.6	46.5	1354	1.2	60.
08429	7.01	15.1	40.8	. 1363	3.1	. 22
08430	7.01	15.0	38.3	1233	۳.	.02
08431	6.62	15.0	36.6	1115	9.	. 04
MEDN	96.9	15.4	40.0	1317	1.4	.10
5.0.	.629	. 45	4.06	116.2		650.

APPENDIX 6
INDIVIDUAL CCINICAL HEMATOLOGY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS
WEEK 4 FEMALES

-						
AN I MAL NUMBER	RBC M1/UL	HGB G/DL	HCT ≈	PLATELET TH/UL	RETIC % RBC	A RETIC
1 1 1	-	1		1	1	1 1 1 1 1 1
GROUP: 3	DOSE LEVEL:	: 200	DOSAGE	E UNIT: MG/KG	⁄KG	
08462	6.19	15.1	36.0	1300	1.3	80.
08463	7.87	16.0	44.6	1318	1.2	60.
08464	7.42	. 15.9	41.6	1358	9.	.04
08465	6.50	15.6	39.2	1174	1.1	.07
08466	6.64	16.5	38.8	1322	1.0	.07
08467	7.87	16.0	46.5	1186	1.0	80.
08469	7.21	14.2	40.8	1434	1.0	.07
08470	6.95	14.5	39.0	1161	1.0	20.
08471	6.26	15.2	35.8	1043	9.	.04
08472	6.46	14.6	36.6	1463	1.0	. 06
MEAN	6.94	15.4	39.9	1276	1.0	.07
S.D.	069.	.76	3.57	132.1		.016
GROUP: 4	DOSE LEVEL:	900	DOSAGE	: LIND	MG/KG	
08502	6.85	15.0	37.8	1201	1.2	80.
08503	6.21	15.2	33.6	1252	1.2	.07
08504	6.63	15.2	37.2	1353	1.2	. 08
90580	6.16	14.3	34.1	1406		90.
08507	5.84	16.2	35.4	1086	1.8	.11
08508	6.61	15.3	36.6	1206	1.4	60.
08509	5.26	14.8	30.1	1118	٥.	. 05
08510	7.01	15.6	38.5	. 1243	1.8	.13
08511	6.90	16.5	38.7	1329	o.	90.
08512	6.72	15.3	37.6	1271	1.4	60.
MEAN	6.42	15.3	36.0	1247	1.3	80 .
s.D.	. 550	.64	2.70	100.1	33	.024

APPENDIX 6
INDIVIDUAL CEINICAL HEMATOLOGY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS
WEEK 4 FEMALES

ANIMAL NUMBER	WBC TH/UL	BLAST TH/UL(%)	META TH/UL(%)	BAND TH/UL(%)	SEG TH/UL(%)	LYMPH TH/UL(%)	MONO TH/UL(%)	EOSIN TH/UL(%)	BASO TH/UL(%)
GROUP: 1	DOSE LEV	EUEL: 0	DOSAG	DOSAGE UNIT: MG/KG	/KG				
0					2 4710)	10 3(20)			(9) (0)
28480	13.0				7.7(10)				
08383	8.0				1.7(21)	6.1(76)			٠
08384	6.6				1.0(10)	8.6(87)			
08385	13.9	(0)0	(0)0'		4.2(30)	9.5(68)			
08386	16.6	(0)0.	(0)0.	(0)0.	2.0(12)	14.6(88)	(0)0.	(0)0.	.0 00.
08387	16.2				2.6(16)	13.3(82)			
08388	13.4				2.0(15)	11.0(82)			
99.60	14.2				1.6(11)	12.1(85)			
08390	21.1			(0)0'	2.3(11)	18.6(88)			
105.00	1 10		(0)0		2.3(17)	10.9(81)	.10 1)	.1(1)	(0)0.
1.000	•				 	i			
MEAN	14.0	0.	0.	0.	2.2	11.5	.1	٠,	0.
S.D.	3.60	.00	.00	.03	.84	3.45	.11	.13	00.
GROUP: 2	DOSE LEV	/EL: 100	D0SAGE	E UNIT: MG/KG	/KG				
08422	10.5		(0)0'	(0)0.	2.5(24)	7.6(72)			.0(0)
08423	13.1	(0)0.			1.3(10)	11.5(88)			
08424	11.9	(0)0.			1.8(15)	9.9(83)			
08425	15.1	(0)0.	(0)0'	(0)0.	3.8(25)	11.2(74)	0 00.	.2(1)	(0)0.
08426	14.3				.7(5)	13.3(93)			
08427	22.7				2.5(11)	19.1(84)			
08428	16.6		(0)O.		1.3(8)	14.6(88)			
08429	12.0				3.0(25)	9.0(25)			
08430	11.1		(0)0.		.8(7)	10.1(91)			
08431	10.6	(0)0'	(0)0.	(0)0.	1.3(12)	9,1(86)	(0)0.	.2(2)	(0)0.
Z U	а Н	c	c	-	9	11.5	,	2.	0
HI.	ם נ	- 6				7 7 4	:-	: 5	٥
S.D.	3.72	00.	9 7.	99.	70.1	7.31	,1 .	17.	5

APPENDIX 6
INDIVIDUAL CLINICAL HEMATOLOGY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS
WEEK 4 FEMALES

BASO TH/UL(%)					(0)0.						(0)0.	0.	00.		(0)0.	(0)0.			(0)0.			(0)0.			C	00.
EOSIN TH/UL(%)					.0 O		.2(1)				0000	5.	.21		.1(1)				(0)0.					(0)0.	c.	. 18
MONO TH/UL(%)					.3(2)			.3(2)			.3(2)		.14		.3(3)				(0)0.			.1(1)			c,	.21
LYMPH TH/UL(%)		8.7(85)	7.8(77)	8.8(26)	10.7(85)	16.8(89)	14.6(91)	12.9(84)	11.0(88)	17.7(91)	12.7(78)	12.2	3.41		8.4(86)	13.0(92)	15.8(85)	9.6(79)	13.0(94)	12.4(77)	17.5(96)	12.6(87)	15.8(88)	11,7(87)	13.0	2.81
SEG TH/UL(%)	/KG	1.0(10)	2.1(21)	2.4(21)	1.6(13)	2.1(11)	1.1(7)	1.5(10)	1.4(11)	1.8(9)	3.3(20)	1.8	.68	ЖG	1.0(10)	1.0(7)	2.2(12)	2.4(20)	(9)8.	2.6(16)	.4(2)	1.6(11)	2.0(11)	1.3(10)	1.5	. 75
BAND TH/UL(%)	DOSAGE UNIT: MG/KG				(0)0.			.0(0)			(0)0.	0.	.03	. UNIT: MG/KG	(0)0.	(0)0.			(0)0.						a	00.
META TH/UL(%)	DOSAGE		(O) (O)				(0)0.			(0)0.	(0)0:	0.	. 00	DOSAGE	(0)0.				(0)0.						0.	00.
BLAST TH/UL(%)	il: 200	.0 0.						0 0.				0.	.00	L: 800	(0)0.				(0)0'						0,	00.
WBC TH/UL	DOSE LEVEL:	10.2	٠	•	•	•	•	15.4				14.3	3.40	DOSE LEVEL:	9.6	14.1			13.8					13.4	14.9	2.86
ANIMAL NUMBER	GROUP: 3	08462	08463	08464	08465	08466	08467	08469	08470	08471	08472	MEAN	S.D.	GROUP: 4	08502	08503	08504	90580	08507	80 580	08209	08510	08511	08512	MEAN	s.0.

APPENDIX 6
INDIVIDUAL CLINICAL HEMATOLOGY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS
WEEK 4 FEMALES

1 DOSE LEVEL: 0 1	AN I MAL NUMBER	POLY	TARGET	ECHINO	ACANTH	H380DY	POIK	NRBC
: 2 DOSE LEUEL: 100 : 2 DOSE LEUEL: 200 : 3 DOSE LEUEL: 200 : 4 + + + + + + + + + + + + + + + + + +		OOSE LEV	1	ı	GE UNIT: MG.	,×G		
1		} - 1	ı	4	ı	ı	ı	
1. 1. 1. 4. 1. 4. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1.			1 +	* *	ı	•	ı	
: 2 DOSE LEVEL: 100 : 2 DOSE LEVEL: 100 : 3 DOSE LEVEL: 200 : 4 + + + + + + + + + + + + + + + + + +	•	- 亡	• •	4	1 1	1 1		1 1
1 - 11+ 1 - 14+ 1 - 15+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17+ 1 - 17		· ;- -		4.		1	1	
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1	•	-	•	*	1	•	ı	•
: 2 DOSE LEVEL: 100 T	_	_	1	4	•	•	1	i
: 2 DOSE LEUEL: 100 T		-	ı	++	1	ı	ı	1
T		DOSE LEV		DOSA	GE UNIT: MG.	'KG		
T 4+ T 4+ T 4+ T 4+ T 4+ T 4+ T 3+ T 4+ T -		-		4	,	ı	,	i
T 4+ T 4+ T 4+ T 3+ T 3+ T 4+ T 3+ T 4+ T 4+ T		–	•	4	ı	1	1	1
T 4+ T 4+ T 4+ T 3+ T 3+ T 4+ T - 4+ T		-	ı	4	ı	•	1	,
T 44.		-	ı	• •	ı	,	ı	,
T 4+ T 5+ T - 5+ T - 7+ T - 7+		-	ı	.	1	•	ı	1
T 5 + 4 + 1		-	1	•	1			
T - 44. T - 74. T - 44. T - 44. T - 44. T - 44. T - 7 - 44.		_	,	3 +	,	•	•	ı
T - 7 4+ T - 7 4+ T -		-	1	. +4	ı	,		
1		-	1	÷	1	,	,	ı
: 3 DOSE LEVEL: 200 T - 44+ T T T + 44+ T T - 44+ T T - 44+		-	•	.	1	ı	ı	ı
· · · · · · · · · · · · · · · · · · ·	m 	DOSE LEV		DOSA	GE UNIT: MG	, KG		
++++++++++++++++++++++++++++++++++++++		۰	•	4	i	1	1	ı
₩ 7 1 1 1 1 1 # + + + + + + + + + + + + + + + + + + +		-	•	4+	•	ı		
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		-		4+	•	1	•	•
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-		_		3+	1	ŧ	•	1
-		_	1	*	1		-	ı
- +		-	1	4+	1	ı	1	
1+ T 4+		_	•	4+	•	ı		•
		‡	-	• 4	1	i	1	1

APPENDIX 6
INDIVIDUAL CÉINICAL HEMATOLOGY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS
WEEK 4 FEMALES

ANIMAL NUMBER	POLY	r TARGET	ECHIND	ACANTH	нзвору	POIK	NRBC
	1 1 1	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	1 1 1 1	1 1 1 1 1 1 1	! ! !	
GROUP: 4	DOSE	DOSE LEVEL: 800	DOSAG	DOSAGE UNIT: MG/KG	/KG		
08502	-	ı	• 4	1	1	ı	
08503	-	ı	++	ı	FEW	•	. 1
08504	_	:	•		•	,	1
08506	_	•	4+	1		,	ı
08507	-		4+	1	1		1
08508	-		44			ı	1
08509	⊢			1	•		ı
08510	-					,	,
08511	-		++	ı	1	•	,
08512	-	ı	4	1		1	

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APPENDIX 6
INDIVIDUAL CLINICAL HEMATOLOGY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS
LAFEK 13 FEMALES

	A RETIC MI/UL		.12	.20	.12	. 04	.13	.03	.04	.07	. 02	. 08	90.	.057			.17	.26	90.	.07	10.	. 05	.02	.05	90.	.03	. 09	.074
	RETIC % RBC	ഥ	1.5	2.4	1.5	į,	1.6	4.	ĸ.	œ.	.2	1.0	1.0	69.	ن	9	2.1	3.2	۲.	٥.	1.2	9.	ĸ.	9.	`.	ĸ.	1.1	.92
SUBCHRONIC TOXICITY STUDY IN RATS WEEK 13 FEMALES	PLATELET TH/UL	ENT.	1246	1127	1086	1019	1094	1121	1147	1015	1468	1094	1142	132.0	3// 3# · #11#1		1141	1206	1141	1275	1175	1152	1187	1333	1067	882	1156	121.5
XICITY STUD 13 FEMALES	ECT.	DOSAGE	44.9	44.5	44.7	40.2	44.5	44.7	42.2	45.2	42.9	41.9	43.6	1.67	00000	DUSHGE	42.6	41.9	44.4	43.6	46.0	42.8	44.2	42.1	44.3	44.4	43.6	1.28
CHRONIC TOXIO	HGB G/DL	1	15.5	15.6	16.1	14.1	16.3	16.2	14.8	15.9	15.3	15.1	15.5	69.		100	15.1	15.3	16.2	15.6	16.7	15.5	15.6	15.1	15.6	16.0	15.7	.50
ens	RBC I/UL	DOSE LEVEL:	8.20	9.16	8.15	7.74	8.39	8.59	7.91	8.36	8.13	7.89	8.15	.256		DOSE LEVEL:	7.88	7.99	8.27	8.13	8.38	7.99	7.83	7.86	8.58	8.37	8.13	.260
	ANIMAL NUMBER	GROUP: 1	08382	08383	08384	08385	08386	08387	08388	08389	08390	08391	MERN	S.D.		GROUP: 2	08422	08423	08424	08425	08426	08427	08428	08429	08430	08431	MERRI	S.D.

APPENDIX 6
INDIVIDUAL CLINICAL HEMATOLOGY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS
WEEK 13 FEMALES

ANIMAL NUMBER	RBC MI/UL	HGB G/DL	HCT *	PLATELET TH/UL	RETIC % RBC	A RETIC MI/UL
GROUP: 3	DOSE LEVEL:	L: 200	DOSAG	DOSAGE UNIT: MG/KG	'KG	
08462	7.72	15.4	42.3	1057	1.9	.15
0846 <i>3</i> 08464	8.48 8.68	16.1 16.6	44.3 45.7	1450 1126		
08465	7.92	15.6	44.3	1199	2.4	. 19
08466	8.53	16.7	47.1	1178	2.3	.20
. 08467	•	15.5	44.4	784	1.5	.12
08469	8.23	15.1	42.3	1484	9.	.05
08470	8.20	15.5	43.1	1057	۲.	90.
08471	8.19	15.8	44.3	1220	9.	.05
08472	8.29	15.5	44.0	1283	4	.03
MEAN	8.23	15.8	44.2	1184	1.2	60.
S.D.	.290	. 53	1.46	202.1	. 78	.064
GROUP: 4	DOSE LEVEL:	L: 800	DOSAGE	: UNIT: MG/KG	,KG	
08502	8.34	15.8	44.0	1070	1.9	. 16
08503	7.79	14.4	40.4	1164	1.9	. 15
08504	7.84	15.8	41.9	1376	2.0	. 16
90580	7.53	14.0	38.0	1234	1.3	.10
08507	7.83	15.3	43.5	1047	2.5	.17
08208	8.05	15.1	42.2	1145	۲.	90.
08209	7.91	15.4	42.8	1175	۲.	90.
08510	•	16.3	45.3	. 972	ī.	. 04
08511	8.58	16.6	45.7	1289	Φ.	.07
.08512	8.36	15.8	43.8	1167	ĸ.	.03
MEAN	8.08	15.4	42.8	1164	1.2	.10
s.D.	.367	08.	2.30	118.0		.055

APPENDIX 6
INDIVIDUAL CLINICAL HEMATOLOGY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS
WEEK 13 FEMALES

	BASO TH/UL(%)						(0)0:					(0)0.		o :	00.				(0)0.								0.	.00
	EOSIN TH/UL(%)						.2(2)						,	-; [;]	.13				.6(4)						.1(1)		'n.	.28
	MOND TH/UL(%)		.1(1)	.1(1)			(0)0.				(0)0.	(0)0.		٠٦.	.10				.3(2)									.13
	LYMPH TH/UL(%)		9.9(89)	8.0(74)	12.3(79)	7.5(77)	7,5(76)	12.6(92)	9.3(81)	10.9(89)	10.6(90)	9.2(77)		8.6	1.84		10.7(85)	11.5(90)	11.1(20)	(69)9.9	10.1(77)	14.7(86)	9.7(84)	9.4(78)	7.5(91)	10.3(78)	10.2	2.21
	SEG TH/UL(%)	/KG	1.0(9)	2.5(23)	2.7(17)	2.1(22)	2.2(22)	1.0(7)	2.1(18)	1.2(10)	.8(7)	2.8(23)		1.8	.76	/KG	1.8(14)	(9)8.	3.8(24)	2.9(31)	2.8(21)	1.9(11)	1.0(9)	2.2(48)	.7(8)	2.8(21)	2.1	1.03
-	BAND TH/UL(%)	DOSAGE UNIT: MG/KG	(0)0.		(0)0.	ĕ	ŏ		(0)0.			(0)0.		0.	00.	E UNIT: MG/KG	(0)0.		(0)0.								C	.03
	META TH/UL(%)	00SAG	(0)0'		(0)0.			(0)0.				(0)0'		٥.	00.	DOSAGE	.0000.		(0)0.							(0)0.	c .	00.
	BLAST TH/UL(%)	EVEL: 0	(0)0.				(0)0.		(0)0.					٥.	00.	EVEL: 100	(0)0.									(0)0.	-	00.
	WBC TH/UL	DOSE LEVE	11.1	10.8	15.6	6.6	6.6	13.7	11.5	12.3	1.8	12.0	ı	11.8	1.76	DOSE LEVE	12.6	12.8	15.9	9.5	13.1	17.1	11.5	12.1	8.2	13.2	1.0	2.63
	ANIMAL NUMBER	GROUP: 1	08382	08383	08384	08385	08386	08387	8838B	08389	08390	08391	! !	MEAN	S.D.	GROUP: 2	08422	08423	08424	08425	08426	08427	08428	08429	08430	08431	1400	S.D.

APPENDIX 6
INDIVIDUAL CCINICAL HEMATOLOGY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS
WEEK 13 FEMALES

				WELLY 17					
ANIMAL NUMBER	WBC TH/UL	BLAST TH/UL(%)	META TH/UL(%)	BAND TH/UL(%)	SEG TH/UL(%)	LYMPH TH/UL(%)	MONO TH/UL(%)	EOSIN TH/UL(%)	BASO TH/UL(%)
GROUP: 3	OOSE LEV	LEVEL: 200	903AG	DOSAGE UNIT: MG/KG	/KG				
08462	7.9	(0)0.	(0)0.	(0)0.	.5(6)	7.3(92)	(0)0.	J	(0)0.
08463	10.5				(9)9.	9.7(92)		.1(1)	
08464	11.3	(0)0.		0 00.	2.3(20)	8.9(29)	(0)0.		0000
08465					.7(8)	8.5(91)			
08466	16.9				3.2(19)	13.0(77)			
08467			(0)0.		1.7(13)	11.5(86)			
08469	9.0				.3(4)	7.6(95)		.1(1)	
08470					1.7(12)	12.6(87)			
08471	18.1				1.8(10)	16.1(89)			
08472	12.9				3.1(24)	9.8(26)			
AEAN	12.3	٠.	۰.	۰.	1.6	10.5	۰.	Ξ.	0.
s.D.	3.53	00.	00.	00.	1.06	2.78	-02	.14	00.
GROUP: 4	DOSE LEVEL:	EL: 800	DOSAGE	E UNIT: MG/KG	⁄KG				
08502	11.9	(0)0.	(0)0.	(0)0.	2.1(18)	9.4(79)	.2(2)	.1(1)	(0)0.
08503	B.2	(0)0.	(0)0.		2.2(27)	5.7(70)	.1(1)		(O)O.
08504	17.2	(0)0.	(0)0.	(O)O.	3.1(18)	13.9(81)			
98596	15.9		(0)0.		5.9(32)	9.4(59)			
08207	14.6	(0)0.		00.00	5.4(37)	8.9(61)	.1(1)	.1(1)	(0)0.
08508	11.8	(0)0:	(0)0.		2.6(22)	9.1(77)			(0)0.
08509	-				1.1(8)	12.9(90)	(0)0.		
08510	11.4				1.1(10)	9.9(87)			
09511					1.8(9)	17.6(90)			
08512	11.7	(0)0.	(0)0'	(0)0'	1.3(11)	10,1(86)	(0)0.		(0)0.
METON	13.7	-	c	c		10 7	-	c	-
֓֞֞֜֜֞֜֜֞֜֜֓֓֓֓֓֓֓֓֓֞֜֜֜֓֓֓֓֓֓֓֡֓֞֜֓֓֓֓֞֜֜֓֓֡֓֞֡֓֓֡֓֞֡֓֡֓֡֓֞֡֓֡֓֜֡֓֜֡֡֜֜֡֡֡֜֡֓֜֡֡֡֡֜֜֡֓֜֡֡֜֜֡֡֜	7.7.	. 6	•			\	•		
ÿ.	7.75	٥٥.	9 0.	.	1./1	J. 7.	9		3.

APPENDIX 6
INDIVIDUAL CLINICAL HEMATOLOGY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS
WEEK 13 FEMALES

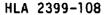
	SUBCHR	SUBCHRONIC TOXICITY STUDY WEEK 13 FEMALES		IN RATS	
NIMA	POLY	TARGET	ECHINO	ACANTH	POIK
CROUP: 1	DOSE LEVEL	0 : 13	DOSAGE	UNIT: MG/	9
5					
08382	-	1	-	•	1
08383	- 1	1	1 1		1
08384	⊢ 1	;	- +		
08385	⊢ :	•	- - F		
98780	þ	ı	_	· ·	
78480	 }-	ŧ.	ı 1-	1 1	
00/00	- 1-		• 1	•	
08390			-		1
08391	-	ł	ı	1	•
GROUP: 2	DOSE LEVEL	EL: 100	DOSAGE	UNIT: MG/KG	9)
08422	<u>+</u>	ı	-	1	
08423	· -	,			
08424	· -	,	_	•	
08425	-	1	-	•	
08426	-	1	_	•	
08427	-	1	-		
08428	-	1	-	•	
08429	_	1	-		t
843	_	•	_	1	
08431	-	1	i .	ı	·
GRÖUP: 3	DOSE LEVEL	EL: 200	DOSAGE	: UNIT: MG/KG	9)
08462	-	ı	-	•	
08463	-	1	_	•	
08464	-	1	_	•	
08465	_	1	_	•	
08466	_	•	_	•	
08467	-	•	1		
08469	-	ı	_		_
08470	-	ŀ	-	•	•
08471	-	ı	_	,	•
08472	-	ı	•		

	/ VALUES	RATS	
APPENDIX 6	INDIVIDUAL CLINICAL HEMATOLOGY VALUES	SUBCHRONIC TOXICITY STUDY IN RATS	WEEK 13 FEMALES

ANIMAL NUMBER	POLY	TARGET	ECHINO	ACANTH	POIK
GROUP: 4	DOSE LEVEL: 800	EL: 800	DOSAGE	DOSAGE UNIT: MG/KG	ĶĢ
08502	-	1	-	1	,
08503	-	1	+	•	•
08504	-	ı	+	1	•
90480	-	,	_	1	,
08507	}	•	-	,	1
08508	-	1	_		
60 580	-	1	-	•	
08510	_		_	1	1
08511	-		_	•	
08512	 -		•	,	,

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APPENDIX 7 Individual Clinical Chemistry Values





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KEY TO CLINICAL CHEMISTRY

H1 = Trace Hemolysis

H2 = Slight Hemolysis

H3 = Moderate Hemolysis

H4 = Marked Hemolysis

H5 = Severe Hemolysis

. APPENDIX 7
INDIVIDUAL CEINICAL CHEMISTRY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS
WEEK -1 MALES

LDH		671	523	7.70	60 2	8 1	372	255.5
ALK P		295	9BT	180	143	203	201	2,95
PLT U/L		41	57	28	21	25	28	7.8
AST U/L		196	7	62	83	9	96	56.7
T CHOL MG/DL	UNIT:	54	69	문	9	81.	89	11.5
GLUCOSE MG/DL	DOSAGE	125	88	82	96	20	92	20.6
CREAT (MC/DL	BASEL INE	1.0	۰.	9.	9.	v.	۲.	. 18
BUN MG/DL	DOSE LEVEL:	23	13	12	14	12	15	4.7
ANIMAL NUMBER	GROUP: 5	08522 H1	08523	08524	08525	08526	MERN	S.D.

APPENDIX 7
INDIVIDUAL CEINICAL CHEMISTRY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS
WEEK -1 MALES

•										
SOD LUM MMOL/L		POTAS MMOL/L	CHLOR 10E MMOL/L	T PROT G/OL	ALBUMIN G/DL	GLOBULIN G/DL	A/G RATIO	CALCIUM MG/DL	IN PHOS MG/DL	T BILI MG/DL
1	•	1 1 1 1 1 1	. ! ! ! ! ! ! ! ! ! ! !		 	1 1 1 1 1 1 1	1	 	1 1 1	
DOSE	JOSE LEVEL: BASELINE	BASEL II	JE DOSAGE	: UNIT:						
14	9.6	6.86	107.3	6.3	4.3		2.15	10.8	13.5	
14	4.7	6.32	101.4	5.2	3.5		2.06	9.7	10.2	•
14	4.4	6.34	103.0	5.8	3.7		1.76	10.2	11.8	Ξ.
14	5.4	6.97	104.2	5.9	4.0		2.11	10.6	12.3	.2
14	145.2	6.57	101.1	9.6	3.7.	1.9	1.95	10.5	11.4	.2
14	145.9	6.61	103.4	5.8	3.8		2.01	10.4		7:
	2.13	.296		.40		.15	.157			. 08

APPENDIX 7
INDIVIDUAL CEINICAL CHEMISTRY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS
WEEK 4 MALES

T B1L1 MG/DL		-		٠.	. o.	 !	۲.	۲.	. 05		۰.	٥.	٠.	Ξ.	0.	٠.	Θ.	0.	٥.	.2	۰.	.07
IN PHOS		7.7	10.2	10.7	. o.	8.5	9.0	6.8	1.02		8.8	7.6	10.0	8.5	8.9	9.6	9.1	9.5	8.8	9.0	8.8	.64
CALCIUM MG/DL		10.3	B. 0. 04	10.5	10.1	10.0	10.2	10.0	.33		9.3	9.7	6.6	10.0	10.4	10.2	10.1	10.8	10.4	10.2	10.1	. 41
A/G RATIO		1.95	1.71 1.71	1.60	1.76	1.90	1.67	1.80	.128		1.81	1.67	2.16	2.39	2.11	1.56	1.90	2.21	1.50	1.65	1.90	.307
eraeurin 6/DL Ni		2.5	, c, c,	2.5	2.1 2.1	2.0	2.1	2.1	. 18		2.1	2.4	1.9	1.8	1.9	2.5	2.0	1.9	2.4	2.3	2.1	.26
ALBUMIN G/DL	9	4.E.	7 K 4	4.0	, r.	3.8	3.5	3.8	.23	9)	3.8	4.0	4.1	4.3	4.0	3.9	3.8	4.2	3.6	3.8	3.9	.21
T PROT G/DL	DOSAGE UNIT: MG/KG	8. K.		, , ,	5.8	. S	5.6	6.0	. 36	UNIT: MG/KG	5.9	6.4	6.0	6.1	6.6	6.4	5.8	6.1	9.9	6.1	6.1	.20
CHLORIDE MMOL/L	DOSAGE	103.4	105.8 105.8 107.7	107.7	102.6	100.1	102.5	104.5	3.21	DOSAGE	108.0	108.8	106.6	104.9	105.7	102.8	105.0	100.8	101.1	102.8	104.6	2.74
POTAS MMOL/L	L: 0	5.49	6.27 6.46 85	6.71	6.20	6.06	6.07	6.01	.521	.: 100	6.05	09.9	6.20	6.33	6.09	6.36	6.36	6.51	6.05	6.51	6.31	.201
SOD I UM MMOL/L	DOSE LEVEL:	151.0	147.9 148.9	148.9	146.1	148.8	148.8	148.0	1.56	DOSE LEVEL:	146.2	147.1	148.8	145.1	148.5	147.0	145.0	147.7	145.5	146.4	146.7	1.34
ANIMAL NUMBER	GROUP: 1	08362 H2 08363	08369 H1 08365 H1 08366 H1	08367H1	08369	08370	08371	MEAN	S.D.	GROUP: 2	08403	08404 H1	08405	08406 H1	08407	08408 H1	08409	08410	08411	08412	MEAN	S.D.

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APPENDIX 7
INDIVIDUAL CEINICAL CHEMISTRY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS
WEEK 4 MALES

				3		3				
ANIMAL NUMBER	SODIUM	POTAS MMOL/L	CHLORIDE MMOL/L	T PROT G/DL	ALBUMIN G/DL	GLOBULIN GLOBULIN	A/G RATIO	CALCIUM MG/DL	IN PHOS	T BIL! MG/DL
GROUP: 3	OSE L	EL: 200	DOSAG	DOSAGE UNIT: MG/KG	Ϋ́G					
08442	147.1	5.85	103.8	6.2	4.0	2.2	1.82	4.6	7.7	0.
08443	148.2	6.10	107.4	6.6	4.0	1.9	2.11	9.6	8.3	:
09444	148.8	6.57	100.8	6.2	3.9	2.3	1.70	10.2	9.5	0.
08445	149.7	5.86	104.1	9.0	3.9	2.1	1.86	6.6	7.8	
08447 H1	148.4	6.40	107.5	5.2	3.9	1.8	2.17	10.1	9.5	0.
08448	147.4	6.83	102.0	5.8	3.7	2.1	1.76	10.5	10.3	1.
08449	146.4	6.47	102.8	5.8	3.6	2.2	1.64	10.4	9.5	0.
08450	146.0	69.9	103.4	6.2	3.8	2.4	1.58	10.4	8.8	
08451	146.3	6.47	103.4	5.7	3.7	2.0	1.85	10.3	4.6	•
08452	144.7	6.50	105.2	0.9	3.7	2.3	1.61	10.0	9.0	.
MEAN	147.3		104.0	5.9	3.8	2.1	1.81	10.1	8.9	0.
S.D.	1.50	.333	2.15	.20	.14		.200	.34	.82	. 05
GROUP: 4	DOSE LEVEL:	EL: 800	DOSAGE	: UNIT: MG/KG	KG	•				
08482	147.2	6.57	109.1	5.7	3.9	1.8	2.17	8.6	9.3	6
08483	148.9	6.13	108.8	5.8	3.7	2.1	1.76	6.6	8	
08484 H1	148.8	6.62	106.1	6.1	4.0	2.1	1.90	6.6	6.6	0.
08485	147.9	6.52	104.4	9.9	4.1	1.9	2.16	10.2	6.7	Ξ.
08486 H2	148.8	69.9	103.2	5.8	3.9	1.9	2.05	6.6	9.0	٦.
08487 H1	144.8	6.03	106.1	5.7	3.6	2.1	1.71	10.2	10.4	0.
08488	146.2	6.27	102.8	6.0	3.4	5.6	1.31	10.4	8.5	0.
08489	148.7	7.03	105.5	5.8	3.9	1.9	2.05	9.6	10.1	۲:
08490	147.9	98.9	8.66	6.0	3.9	2.1	1.86	10.3	9.0	٥.
08491	147.0	6.87	104.1	6.1	3.8	2.3	1.65	10.3	9.6	0.
MEAN	147.6	94.9	105.0	5.9	3.8	2.1	1.86	10.1	9.1	0
s.D.	1.34	.330	2.79	.16	.20	.23	.266	.23	.85	. 05

APPENDIX 7
INDIVIDUAL CEINICAL CHEMISTRY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS
WEEK 4 MALES

ANIMAL NUMBER	BUN MG/DL	CREAT MG/DL	GLUCOSE MG/DL	T CHOL MG/OL	AST U.C.	ALT .	ALK P	LDH
GROUP: 1	DOSE LEVEL: 0	EL: 0	DOSAGE	DOSAGE UNIT: MG/KG	KG			
08362 H1 08363	12	øó.	94	53	83 82	28 22	206 106	154 538
08364	71 7	, ·	4 6 4 4	69 7	82 6	28 3.0	167	431
08366 H1	1 1		101	4	NO TESTA	MO TESTO	172	NO TEST
08367 H1	10	۲.	77	54	122	39	179	727
08368	11	9.	92	9	74	28	89	241
08369	10	۲.	88	96	69	19	104	261
08370	10	₩.	91	6 9 .	62	24	170	263
08371	13	۲.	84	68	63	23	110	181
MEAN	13	۲.	. 8	62		214	140	1219
S.D.	2.7	.10	8.5	12.0	733.4	592.4	44.1	
GROUP: 2	DOSE LEVE	LEVEL: 100	DOSAGE	DOSAGE UNIT: MG/KG	KG			
08403	12	۲.	85	35	81	28	117	729
08404H1	17	9.	91	55	B Z	24	107	630
08405	15	~	88	38	80	20	131	356
08406 H1	16	۰.	06	73	81	24	26	546
08407	12	٦.	82	84	20	21	114	225
08408H1	11	9.	82	63	81	29	112	711
08409	10	٠.	66	35	81	22	135	979
08410	12	9.	96	29	98	25	122	417
08411	12	۲.	0.6	71	63	26	133	152
08412	11	۲.	87	63	99	24	118	248
MEAN	13	9.	68			24	117	
S.D.	2.3	80.	5.5	14.7	7.6	2.9	17.0	214.4

^a Deleted from statistics (individual value was 2400; mean and s.d. would have been 313 $^{\pm}$ 733.4). ^b Deleted from statistics (individual value was 1900; mean and s.d. would have been 214 $^{\pm}$ 592.4). ^c Deleted from statistics (individual value was 8900; mean and s.d. would have been 1219 $^{\pm}$ 2705.0).

APPENDIX 7
INDIVIDUAL CEINICAL CHEMISTRY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS
WEEK 4 MALES

			3	WEEK 4 MALES				
ANIMAL NUMBER	BUN MG/DL	CREAT MG/DL	GLUCOSE MG/DL	T CHOL MG/DL	AST U/L	F. 7.2	ALK P	52
GROUP: 3	DOSE LEVEL: 200	EL: 200	DOSAG	DOSAGE UNIT: MG/KG	ور			
08442	15	۲.	68	61	78	53	144	405
08443	14	۲.	121	61	6 2	27	132	309
08444	15	۲.	68	45	76	22	124	211
08445	14	۲.	94	20	89	23	98	121
08447H1	14	<u>د</u> .	94	.0 .	84	22	103	430
08448	12	۲.	96	42	82	25	146	782
08449	11	9.	29	62	73	32	118	276
08450	11	۲.	98	ス	9.0	37	199	236
08451	10	œ.	80	47	57	24	191	230
08452	10	۲.	101	69	69	. 23	120	527
MEAN	13		92		74	56	136	352
S.D.	2.0	90. 0	12.9	9.6	9.7	4.9	35.7	192.4
GROUP: 4	DOSE LEVEL:	EL: 800	DOSAGE	DOSAGE UNIT: MG/KG	G			
08482	12	9.	92	58	87	26	0.6	418
08483	11	9.	90	62	55	21	92	214
08484H1	14	9.	81	49	92	29	106	328
08485	15	9.	0.6	77	20	27	110	463
08486 H1	12	ŗ,	96	25	58	33	105	167
08487 H1	13	۲.	82	78	103	33	107	723
08488	. 27	Φ.	25	64	74	23	96	189
08489	15	۲.	94	54	107	35	118	630
08490	9	ζ.	104	28	51	19	106	102
08491	12	ζ,	87	78	66	31	121	506
MEAN	14	9	88	67	29	28	105	374
S.D.	5.3	80.	8.1		20.4	5.5	10.2	209.1

APPENDIX 7
INDIVIDUAL CEINICAL CHEMISTRY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS
WEEK 13 MALES

T BILI MG/DL		.2	?	.2	.2	٠.	.5	.5	?	.2	.2	.2	90.		.2	-:	Τ.	۲.		.2	.5	.2	.5	.2	5.	90.
IN PHOS		8.1	7.7	7.0	8.1	7.8	6.6	9.5	6.7	9.6	9.4	9.6	86.		8.9	6.5	€.9	7.7	7.2	7.7	9.0	9.7	9.3	10.1	8.2	1.25
CALC IUM MG/DL.		10.7	10.2	9.6	10.1	9.8	8.5	4.6	8.6	9.3	6.6	9.6	. 65		9.6	6.6	8. 6	10.1	10.5	9.5	7.6	9.3	10.3	9.3	9.6	. 41
A/G RAT10		1.28	1.50	1.46	1.24	1.19	1.20	1.56	1.63	1.70	1.57	1.43	.190		1.52	1.46	1.21	1.54	1.32	1.58	1.63	1.50	1.31	1.46	1.45	.133
G/DL G/DL		2.9	2.4	2.4	2.9	3.2	3.0	2.5	2.4	2.3	2.3	2.6	. 33		2.5	5.6	2.8	2.6	2.8	2.6	2.4	2.6	2.9	5.6	5.6	.15
LBUMIN	9>	3.7	3.6	3.5	3.6	3.8	3.6	3.9	3.9	3.9	3.6	3.7	.15	9)	3.8	ъ. В.	4.6	4.0	3.7	4.1	3.9	3.9	3.8	3.8	3.8	. 19
T PROT G/DL	UNIT: MG/KG	9.9	0.9	5.9	6.9	7.0	9.9	6.4	6.3	6.2	5.9	6.3	. 35	UNIT: MG/KG	6.3	6.4	6.2	9.9	6.9	6.7	6.3	6.9	6.7	6.4	6.5	.17
CHLOR I DE MMOL/L	DOSAGE	102.5	105.7	103.0	103.3	105.7	101.0	105.7	104.8	103.1	107.7	104.3	2.00	DOSAGE	102.5	102.0	102.5	104.7	100.6	105.1	104.6	103.5	104.8	106.4	103.7	1.75
ŒΣı	0 :	5.25	6.36	5.71	6.83	6.43	6.39	6.91	6.27	6.19	5.74	6.25	.551	-: 100	6.10	6.30	6.26	6.01	6.14	6.39	6.67	6.50	6.15	6.45	6.30	.206
SODIUM	DOSE LEVEL:	143.8	146.8	143.9	145.8	145.1	149.5	146.8	144.1	147.9	147.4	. 146.1	1.91	DOSE LEVEL:	144.8	146.0	142.2	143.4	147.6	147.9	147.9	146.5	146.8	147.1	146.0	1.96
	GROUP: 1	08362	08363	08364	08365 H1	08366	08367	08368	08369	08370	08371	MERN	S.D.	GROUP: 2	08403	08404	08405	09406	08407	08408	08409	08410	08411	08412	MFR	S.D.

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APPENDIX 7
INDIVIDUAL CEINICAL CHEMISTRY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS
WEEK 13 MALES

)				
ANIMAL	SODIUM	POTAS MMOL/L	CHLORIDE MMOL/L	T PROT G/DL	ALBUMIN G/DL	GLOBUL IN G/Ot.	A/G RAT10	CALCTUM MG/DL	IN PHOS	T BILI MG/DL
) 			 	† † † † †	; ; ; ;	! ! ! ! !	 	!	 	1 1 1 1 1
GROUP: 3	DOSE LEVEL:	EL: 200	DOSAGE	DOSAGE UNIT: MG/KG	,KG					
08442	145.0	90.9	103.3	6.3	3.8	2.5	1.52	6.7	6.9	2.
08443	146.3	6.61	103.7	4.9	3.9	2.5	1.56	10.7	7.7	. 2.
08444	143.8	5.98	98.7	6.2	3.5	2.7	1.30	10.1	7.9	
08445	143.2	5.98	99.8	6.5	3.6	2.9	1.24	8.6	5.7	. 2
08447	145.8	5.76	104.2	4.9	3.7.	2.7	1.37	10.2	7.2	
08449	143.5	9.00	106.0	6.5	3.9	2.6	1.50	6.7	8.5	.2
08451	145.9	5.93	106.2	6.2	3.8	2.4	1.58	10.0	9.7	2
08452	148.3	6.76	108.5	4.9	3.B	2.6	1.46	8.6	8.7	7.
08453	145.8	6.43	107.5	6.2	3.6	2.6	1.38	4.6	6.6	. 2
08455	147.3	6.27	104.9	4.9	3.8	2.6	1.46	9.0	10.1	0.
MEAN	145.5	6.18		6.3	3.7	2.6	_	6.7	8.1	
S.D.	1.65	. 325	3.12	. 12	.13	.14	.112	66	1.36	. 08
GROUP: 4	DOSE LEVEL:	EL: 800	DOSAGE	UNIT: MG/KG	KG					
08482	146.4	6.49	101.7	9.9	4.0	5.6	1.54	10.6	7.5	
08483	. 146.0	6.50	105.5	5.8	3.5	2.3	1.52	6.6	0.8	
08484	142.7	6.57	101.9		3.6	2.3	1.57	10.3	0.0	
08485	144.4	6.85	103.7	9.0	3.7	2.3	1.61	10.4	7.7	
08486	145.2	6.79	103.7	6.9	3.8	2.7	1.41	8.6	9.1	.5
08487 H1	146.8	6.51	109.2	9.9	4.1	2.5	1.64	9.5	10.1	.5
08488	145.4	6.57	105.9	5.9	3.0	2.9	1.03	9.0	10.6	.2
08489	148.1	6.72	108.3	6.4	4.2	2.2	1.91	9.1	6.6	.2
08490	147.2	95.9	103:1	6.2	3.9	2.3	1.70	6	6.8	
08492	147.4	6.17	104.0	6.2	3.9	2.3	1.70	9.1	10.8	.2
MEAN	146.0	6.58	104.7	6.2	3.8		1.56	6.7	1.6	C.
s.D.	1.60	.195	2.52	.30	.35	. 23	.230	25.	1.25	. 05

APPENDIX 7
INDIVIDUAL CEINICAL CHEMISTRY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS
WEEK 13 MALES

ANIMAL NUMBER	BUN MG/DL	CREAT MG/DL	GLUCOSE MG/OL	T CHOL MG/DL	AST U/L	F 7	ALK P	LDH LDH
	i c		10000	7 (M.)	ŗ			
GROUP: 1	DOSE LEVEL:	=	UUSAGE	UUSAGE UNI: N6/K6	ð			
08362	12	۲.	100	49	26	23	136	313
08363	12	9.	103	64	69	25	20	172
08364	16	۲.	105	9.0	52	22	06	133
08365 H1	12	9.	123	117	64	25	29	193
08366	18	9.	86	9	77	28	82	524
08367	6	۲.	84	62	73	28	26	137
08368	13	۰,	109	88	52	21	35	131
08369	13	۲.	112	88	51	16	43	219
08370	•	.5	0.6	96	54	27	77	121
08371	12	ĸ.	104	108	96	24	75	207
MEAN	13	Ý	103	8 4	63	24	74	215
	•					F		107 0
S.D.	8.Z	An.	11.6		7.2	7.0		173.0
GROUP: 2	DOSE LEVEL:	L: 100	DOSAGE	UNIT: MG/KG	(9			
08403	12	9.	109	49	57	29	91	221
08404	13	9.	109	89	43	21	9	111
08405	12	9.	112	45	09	20	9.6	259
08406	13	9.	123	109	74	23	20	510
08407	13	9.	110	91	50	16	92	111
08408	10	9.	96	88	7	24	62	556
08409	0	۶.	110	42	96	18	91	196
08410	10	٠.	105	93	55	16	83	289
08411	10	ŗ.	108	109	47	. 41	98	109
08412	13	ĸ.	103	80	64	24	73	143
MEAN	12	٧.	109		58	21	80	251
s.D.	1.6		6.9	24.9	6.6	4.1	14.4	162.1

APPENDIX 7
INDIVIDUAL CEINICAL CHEMISTRY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS
WEEK 13 MALES

ANIMAL	BUN MG/DL	CREAT MG/DL	GLUCOSE MG/DL	T CHOL. MG/DL	AST U/L	ALT U/L	4 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7	로
GROUP: 3	DOSE LEVEL: 200	EL: 200	DOSAGE	E UNIT: MG/KG	·KG			
08442	14	۲.	103	82	99	22	98	302
08443	15	9.	135	93	113	47	95	425
08444	15	۲.	96	20	63	19	74	164
08445	14	۲.	101	26	62	24	. 49	102
08447	16	ĸ.	96	. 62	2%	22	9	320
08449	13	۰.	95	74	85	28	54	909
08451	11	۰.	94	56	52	18	74	205
08452	14	9.	96	78	47	20	49	222
08453	12	9.	112	87	20	39	29	221
08455	11	9	66	61	51	22	71	117
MEAN	14	9.	102					
5.0.	1.7	90	12.7	10.6	20.4	4 9.5	5 15.7	153.3
GROUP: 4	DOSE LEVEL:	EL: 800	DOSAGE	: UNIT: MG/KG	Ϋ́G			
08482	10	5.	108	93	71	32	62	175
08483	13	9.	93	63	63	23	91	300
08484	13	9.	103	72	55	24	9	142
08485	14	9.	66	98	80	45	123	413
08486	12	ē.	66	25	75	38	69	393
08487 H1	14		78	83	94	48	117	389
08488	23	۲.	0.6	51	52	25	118	. 85
08489	11	9.	101	9	. 61	31	82	111
08490	^	٦.	132	88	41	26	25	71
08492	11	ŗ.	102	09	29	35	6	121
MEAN	13		100			33		
s.D.	4.2	. 60	14.0	13.8	15.1	8	3 23.7	138.4
	:		:					

APPENDIX 7
INDIVIDUAL CEINICAL CHEMISTRY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS
WEEK -1 FEMALES

HQ1		680	537	655	. 926	454	580 91.3
PLK P		216	156	140	135	179	165 33.2
ALT U/L		30	21	27	23	28	26 3.7
AST		133	85	96	85	110	102 20.2
T CHOL MG/DL	UNIT:	85	61	8 2	125	25	85 24.1
GLUCOSE MG/DL	DOSAGE	96	85	91	82	87	89 4.4
CREAT 6 MG/DL	BASEL INE	۲.	9.	۰.	Θ.	₩.	.10
BUN MG/DL	DOSE LEVEL:	17	13	17	13	13	15
AN IMAL NUMBER	GROUP: 5	08527 H1	08528	08529	08530	08531	MEAN S.D.

APPENDIX 7
INDIVIDUAL CEINICAL CHEMISTRY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS
WEEK -1 FEMALES

)				
AN I MAL NUMBER	SOD I UM MMOL /L	POTAS MMOL/L	CHLORIDE MMOL/L	T PROT G/DL	ALBUMIN G/DL	GLOBUL IN	A/G RATIO	CALCIUM MG/DL	IN PHOS	T 81L1 MG/OL
1	•	1 1 1 1 1 1		!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!	!		!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!	1 1 1 1	1	1 1 1 1 1 1 1 1 1
GROUP: 5	DOSE LEVEL: BAS	EL: BASELINE	NE DOSAGE UNIT:	CNIT						
08527 H1	147.3	6.67	106.9	5.7	4.0	1.7	2.35	11.2	14.1	.2
08528	143.2	5.76	105.4	5.5	3.8	1.7	2.24	10.2	11.0	
08529	146.6	69.9	108.0	5.8	3.9	1.9	2.05	10.5	11.7	Θ.
08530	145.1	6.77	106.6	6.1	4.2	1.9	2.21	11.3	11.4	Ξ.
08531	145.4	6.73	106.8	6.6	4.0	1.9	2.11	10.4	12.0	0.
MEAN	145.5	6.52	106.7	5.8						
5.0.	1.57			.22	.15		.117	.50		90.

APPENDIX 7 INDIVIDUAL CEINICAL CHEMISTRY VALUES SUBCHRONIC TOXICITY STUDY IN RATS WEEK 4 FEMALES

ANIMAL NUMBER	SOD JUM MMOL/L	POTAS MMOL/L	CHLORIDE MMOL/L	T PROT G/DL	ALBUMIN G/OL	GLOBULIN 6/DL	A/G RATIO	CALCIUM MG/DL	IN PHOS MG/DL	T 81L1 MG/DL
GROUP: 3	DOSE LEVEL: 200	EL: 200	DOSAGE	DOSAGE UNIT: MG/KG	∕KG					
08462	142.8	5.61	107.9	4.9	4.3	2.1	2.05	10.0	8.0	۲.
08463 H1	146.9	6.15	111.4	4.9	4.4	2.0	2.20	10.3	8.3	-:
08464 H1	146.7	96.9	107.2	9.	4.1	1.7	2.41	9.6	10.4	0.
08465	148.0	6, 19	108.2	9.9	4.4	2.2	2.00	10.4	8.7	٦.
08466	147.3	6.37	112.4	6.1	4.1	2.0	2.05	10.1	6. 8	٥.
08467	144.2	5.72	106.0	9.9	4.4	2.2	2.00	10.7	7.3	٠.
08469	143.0	6.09	104.3	6.1	3.8	2.3	1.65	10.4	8.3	- :
08470	145.8	6.10	104.7	6.1	3.8	2.3	1.65	10.5	В	۲.
08471 H1	143.B	5.94	104.7	9.8	3.7	2.1	1.76	9.6	7.9	o.
08472	144.0	6.23	105.2	6.3	3.9	2.4	1.63	8.6	7.6	0
Name	145.2		107.2	6.2	4.1	2.1	1.94	10.2	4.8	г.
S.D.	1.91	.356		.29	. 28	.20		.33	.86	.05
GROUP: 4	DOSE LEVEL:	EL: 800	DOSAGE	E UNIT: MG/KG	κG					
08502	145.4	6.18	109.8	6.4	4.1	2.3	1.78	10.1	7.4	0.
08503	144.7	66.6	105.0	6.0	4.0	2.0	2.00	10.0	8.7	.
08504	145.9	6.08	105.7	5.8	4.0	1.8	2.22	10.3	9.1	o.
90200	145.3	6.26	110.3	6.2	3.9	2.3	1.70	10.1	9.8	
08507	146.9	6.61	104.6	6.3	4.4	1.9	2.32	10.8	9.5	0.
08508	145.1	6.04	103.7	9.0	3.9	2.1	1.86	10.9	8.1	-:
08509 H1	141.4	5.62	106.4	6.9	4.1	1.9	2.16	10.3	9.6	
08510	145.9	6.63	102.3	5.9	3.9	. 2.0	1.95	10.8	 8	.2
08511	146.5	6.00	101.6	9.9	4.2	2.4	1.75	10.6	8.5	-: '
08512	146.6	6.15	103.9	6.4	3.8	2.6	1.46	10.2	7.8	o.
NG LE	145.4		105.3	6.5	4.0	2.1	1.92	10	8.5	.1
5.0.	1.56	.298	2.88	.26		.26	.264		89.	.07

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APPENDIX 7
INDIVIDUAL CLINICAL CHEMISTRY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS
WEEK 4 FEMALES

ANIMAL NUMBER	∟⊒	POTAS MMOL/L	CHLORIDE MMOL/L	T PROT G/DL	ALBUMIN G/DL	CLOBUL IN	A/G RAT10	CALC IUM MG/DL	IN PHOS	T BILI MG/DL
! ! ! !	1 1 1 1 1	1 1 1 1 1	! ! ! !		! ! ! ! ! ! ! ! ! ! ! ! ! ! ! ! ! ! ! !	 	 	 	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	1 1 1 1 1 1 1 1 1
GROUP: 1	DOSE LEVEL:	L: 0	DOSAGE	DOSAGE UNIT: MG/KG	9					
08382	143.2	5.44	109.6	6.0	4.0	2.0.	2.00	9.6	6.9	Θ.
08383	145.9	5.48	108.5	6.3	4.2	2.1	2.00	9.6	6.2	0
08384	148.2	6.20	110.0	6.7	. 5.0	1.7	2.94	10.7	9.7	· •
08385	146.4	5.64	107.9	4.9	4.1	2.3	1.78	10.0	7.7	
98380	149.5	5.60	106.5	6.0	4.1	1.9	2.16	9.6	7.7	
08387.	143.1	5.24	102.8	6.3	4.1	2.2	1.86	10.1	8.2	:
08388	144.0	5.74	102.2	5.9	4.2	1.7	2.47	10.3	7.2	. 2
08389 H1	143.9	6.15	103.1	5.5	3.7	1.8	2.06	9.7	10.3	! -:
06390	142.8	5.71	103.2	5.8	3.7	2.1	1.76	9.6	8	. 5
08391	145.6	5.91	106.3	6.2	3.8	2.4	1.58	10.0	8.4	0.
MEAN	145.3	5.71	106.0	6.1	4.1	2.0	2.06	6.6	8.1	Τ.
s.D.	2.28	.305	2.98	.34	.37	.24	.394	.36	1.23	90.
GROUP: 2	DOSE LEVEL:	L: 100	DOSAGE	UNIT: MG/KG	Ŋ					
08422	144.9	5.55	109.3	6.6	4.0	1.9	2.11	9.5	6.1	1,
08423	146.5	6.03	110.1	6.3	4.1	2.2	1.86	10.2	8.1	! -:
08424	146.9	65.9	106.8	6.3	4.2	2.1	2.00	10.0	8.9	۲.
08425.	145.4	6.16	108.0	7.1	4.7	2.4	1.96	10.7	8.8	0.
08426	147.8	6.40	107.5	5.5	4.0	1.5	2.67	10.0	9.6	0.
08427 H1	141.3	6.16	104.4	5.7	3.7	2.0	1.85	9.6	8.3	9.
08428	143.3	6.06	104.9	6.9	4.3	2.2	1.95	10.3	7.2	.2
08429	144.7	5.46	104.6	6.3	4.0	2.3	1.74	9.7	7.5	0.
08430	144.1	5.62	102.6	6.1	3.9	2.5	1.77	6.6	8.9	
08431	143.2	5.92	105.5	5.8	3.7	2.1	1.76	9.6	7.8	. .
MEAN	144.8	5.99	106.4	6.1	4.1	2.1	1.97	6.6	7.9	0,
S.D.	1.95	.366	2.37	. 46	.30	. 25	.274	.39	1.09	.07

APPENDIX 7
INDIVIDUAL CLINICAL CHEMISTRY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS
WEEK 4 FEMALES

LDH 17		110 505 73 322									01 402	26.3 187.3		44 509									55 292	100 382	
ALT ALK PU/L U/L		27 1										3.9											26	28 16	
AST	9)	% C	78	9	72	93	9.0	118	63	20	82	16.3	وي	106	08	92	84	90	73	90	93	63	63	82	;
T CHOL MG/DL	DOSAGE UNIT: MG/KG	66 63	83	84	.29	て	94	40	26	85		5 14.7	E UNIT: MG/KG	20	83	82	66	28	89	66	74	95	92	74	•
GLUCOSE MG/OL	DOSAG	94	06	100	88	98						8 5.5	DOSAGE (94	16	
CREAT L MG/DL	DOSE LEVEL: 0	17 . 6 118 . 7	14 .6	16 . 6	16 .6	14 .6			13 .7	13 .8		2.9 .08	LEVEL: 100					16		•	-	•	14	7, 71	
R MG/DL	1												2 DOSE											•	
AN I MAL NUMBER	GROUP:	08382	08384	08385	09386	08387	08388	08389	08390	08391	MEAN	S.0.	GROUP:	08422	08423	08424	08425	08426	08427	08428	08429	08430	08431	MEAN	ĺ

APPENDIX 7
INDIVIDUAL CLINICAL CHENISTRY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS
WEEK 4 FEMALES

GROUP: 3 DOSE LE 08462 16 08463 H1 17 08464 H1 16 08465 17 08466 17 08467 11 08467 18 08470 8 08471 H1 8 08472 8 MEAN 13 S.D. 4			70/0F	TIS/ UL	Z	,		
4 DOSE	DOSE LEVEL: 200	_	DOSAGE	DOSAGE UNIT: MG/KG	'KG			
4 DOSE		۲. 9.	0 8 0	91 88	85 69	5 7 7 7 7	111	771
4 DOSE		ŗ.	85	51	83	22	94	513
4 DOSE		ζ.	97	92	71	20	104	338
4 DOSE		Ņ	84	. 98	73	24	92	331
4 DOSE		Ņ	66	66	85	20	119	381
4 DOSE		Ņ	.102	74	92	23	69	223
4 DOSE		в.	77	81	74	31	88	461
4 DOSE		۲.	82	25	9.6	28	100	725
): 4 DOSE		۲.	106	107	81	26	22	343
o: 4 DOSE	٠	۲.	89	83		24	46	442
: 4 DOSE	4.1	. 05	10.0	15.5	10.1	3.5	15.7	179.3
	LEVEL: 800		DOSAGE	DOSAGE UNIT: MG/KG	Ϋ́G			
08502 16		۰.	85	103	90	30	83	379
08503 15		9.	98	74	75	20	51	695
		۲.	. 87	88	20	26	84	272
08506 14		9.	78	95	75	25	50	457
		9.	82	100	73	23	114	180
		Ċ.	82	104	59	24	87	294
		9.	06	89	91	32	126	260
		۲.	. 77	96	. 67	19	96	378
08511 10		۲.	88	115	74	30	20	407
			9.0	101	58	24	60	82
		9.	98	66		25	82	391
S.D. 2.8	60	. 05	4.6	14.3	8.9	4.3	25.4	209.6

APPENDIX 7
INDIVIDUAL CEINICAL CHEMISTRY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS
WEEK 13 FEMALES

		•																									
T B1L1 MG/DL			.5	.2	٠.	.	٣.	.5	.5	~	.2	6		80.		.1	.1	.2	.1	.2	.2	.5	.2	.2	.2	.5	.05
IN PHOS MG/DL		5.5	7.6	7.5	7.2	6.2	7.8	8.3	9.0	7.2	7.6	7.3		<u>6</u>		6.2	7.1	6.1	7.5	9.9	6.B	7.7	9.5	8.5	9.7	7.8	1.32
CALCIUM MG/DL		10.2	10.5	10.1	9.5	6.6	10.5	6.6	6.6	10.1	9.6			.33		10.2	10.4	10.4	10.2	10.3	10.3	10.3	10.3	6.6	6.6	10.2	.18
A/G RAT10		1.72	1.54	1.48	1.31	1.48	1.88	1.48	1.46	1.56	1.56	- -	\\	. 156		1.23	1.60	1.32	1.33	1.64	1.68	1.58	1.96	1.57	1.52	1.54	.211
670L 670L 670L		2.5	5.6	2.5	2.9	2.5	2.5	2.7	2.8	2.7	2.7	•	6.0	.14		3.1	2.5	2.8	2.7	2.5	2.5	2.6	2.3	2.8	2.9	2.2	.24
ALBUMIN (6/DL	9	4.3	4.0	3.7	3.8	3.7	4.7	4.0	4.1	4.2	4.2	•	4.1	.31	9	3.8	4.0	3.7	3.6	4.1	4.2	4.1	4.5	4.4	4.4	1.4	.31
T PROT G/DL	DOSAGE UNIT: MG/KG	6.8	9.9	6.2	6.7	6.2	7.2	6.7	6.9	6.9	6.9		•	.31	UNIT: MG/KG	6.9	6.5	6.9	6.9	9.9	6.7	6.7	6.9	7.2	7.3	4	.31
CHLORIDE MMOL/L	DOSAGE	104.7	103.8	103.5	108.4	106.0	105.9	110.2	109.2	104.8	106.6	,	1.00.2	2.29	DOSAGE	106.2	104.3	104.5	105.8	104.7	105.9	108.1	108.5	105.9	107.9	104.0	1.52
POTAS (.: 200	5.56	6.50	6.22	5.84	5.73	5.74	6.57	5.68	5.43	6.52	ŧ	2.78	.432	. 800	6.19	50.00	6.03	6.43	6.04	6.04	6.02	6.94	6.00	6.50	66.	.314
SOOTUM	DOSE LEVEL: 200	142.5	143.5	145.9	144.2	145.8	143.0	145.2	145.9	144.4	144.0	. ,	144.4	1.23	DOSE LEVEL:	144.1	143.4	145.3	145.7	144.3	142.5	142.7	145.5	145.7	146.7	* * * * * * * * * * * * * * * * * * * *	144.0
ANIMAL NUMBER	GROUP: 3	08462	08463	08464	08465	08466	08467	08469	08420	08.421	08472		Z U	S.D.	GROUP: 4	0.8502	50500	08504	08504	08502	08208	08209	08510	08511	08512	i d	S.D.

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APPENDIX 7
INDIVIDUAL CEINICAL CHEMISTRY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS
WEEK 13 FEMALES

													•	- 160	-											
T BIL1 MG/DL		6	Ξ.	.2	.2	. 5	. 2	. 2.	, m ,	; • ;	.2	6	90.		2.	! -:		.2	.2	.2	.2	-4	.2	.2	~!	90.
IN PHOS		5.8	4.6	7.1	5.5	. 6	8.6	7.5	6	2.9	10.3	7.4	1.95		6.9	7.3	7.0	9.9	8.1	9.7	6.9	7.6	6.9	7.4	7.3	99.
CALCIUM MG/DL		10.3	9.7	8.6	9.7	6.6	10.1	10.0	9.3	8.6	9.4	6	.30		10.1	10.3	6.6	10.2	10.6	9.6	10.2	9.5	10.2	9.4	10.0	.37
A/G RAT10		1.83	1.44	1.58	1.44	1.43	1.84	1.83	1.59	1.56	1.41	1.59	.177		1.63	1.71	1.50	1.42	1.45	1.75	1.76	1.74	1.72	1.70	1.64	.131
GLOBUL IN G/DL		2.3	2.7	2.4	2.7	2.8	2.5	2.4	2.7	2.5	2.9	2.6	.20		2.4	2.4	5.6	3.1	2.9	2.4	2.5	2.3	2.5	2.3	2.5	.26
ALBUMIN G/OL	KG	4.2	3.9	3.8	3.9	4.0,	4.6	4.4	4.3	3.9	4.1	4.1	.26	9	9. N	4.1	٧.9	4.4	4.2	4.2	4.4	4.0	4.3	3.9	4.1	.20
T PROT G/DL	UNIT: MG/	6.9	9.9	6.2	9.9	6.9	7.1	6.9	7.0	6.4	7.0	6.7	.29		6.3	6.5	6.9	7.5	7.1	9.9	6.9	6.3	8.9	6.2	. 6.9	. 41
CHLORIDE MMOL/L	DOSAGE	104.2	106.5	103.0	106.2	106.8	108.1	107.3	104.8	108.1	104.9	106.0	1.71	DOSAGE	108.0	106.0	103.5	109.1	106.8	108.8	107.7	109.2	103.1	105.7	106.8	2.20
POTAS MMOL/L	0 :-	5.75	5.82	6.32	5.81	5.85	6.53	6.18	94.9	6.84	5.90	6.16	.388	.: 100	6.27	5.93	6.58	5.80	6.70	5.96	6.00	5.88	5.93	6.32	6.14	.313
SOD I UM MMOL/L	DOSE LEVE	143.4	143.4	145.7	142.2	145.2	143.9	144.9	145.1	144.2	146.6	144.5	1.29	DOSE LEVEL	145.2	144.2	144.5	142.9	147.0	145.2	143.6	147.2	145.1	144.8	145.0	1.34
ANIMAL	GROUP: 1	08382	08383	08384H1	08385	98280	08387H1	08388	08389	08390	08391	MEAN	S.D.	GROUP: 2	08422 H1	08423 Hl	08424H2	08425	08426	08427HI	08428	08429	08430	08431	MEAN	S.D.
	SODIUM POTAS CHLORIDE T PROT ALBUMIN GLOBULIN A/G CALCIUM IN PHOS T MMOL/L MMOL/L MMOL/L G/DL G/DL G/DL RATIO MG/DL M	SODIUM POTAS CHLORIDE T PROT ALBUMIN GLOBULIN A/G CALCIUM IN PHOS MMOL/L MMOL/L MMOL/L G/DL G/DL RATIO MG/DL MG/DL 1 DOSE LEVEL: 0 DOSAGE UNIT: MG/KG	L SODIUM POTAS CHLORIDE T PROT ALBUMIN GLOBULIN A/G CALCIUM IN PHOS T RMOL/L MMOL/L MMOL/L G/DL G/OL G/DL RATIO MG/DL M HG/DL MG/DL M HG/DL MG/DL M HG/DL M HG	R MMOL/L MMOL/L MMOL/L G/DL G/OL G/OL RATIO MG/DL MG/D	L SODIUM POTAS CHLORIDE T PROT ALBUMIN GLOBULIN A/G CALCIUM IN PHOS T MOL/L MMOL/L G/DL G/OL G/DL RATIO MG/DL MG/D	L SODIUM POTAS CHLORIDE T PROT ALBUMIN GLOBULIN A/G CALCIUM IN PHOS T MIOL/L MMOL/L MMOL/L G/OL G/OL G/OL RATIO MG/DL MG	L SODIUM POTAS CHLORIDE T PROT ALBUMIN GLOBULIN A/G CALCIUM IN PHOS T MOL/L MMOL/L G/OL G/OL RATIO MG/DL MG/	L SODIUM POTAS CHLORIDE T PROT ALBUMIN GLOBULIN A/G CALCIUM IN PHOS T BILITALIA MMOL/L MMOL/L G/DL G/OL G/DL G/DL G/DL G/DL G/DL G/DL G/DL G/D	SODIUM POTAS CHLORIDE T PROT ALBUMIN GLOBULIN A/G CALCIUM IN PHOS T BIL	SODIUM POTAS CHLORIDE T PROT ALBUMIN GLOBULIN A/G CALCIUM IN PHOS T BILL MMOL/L HMOL/L G/DL G/DL G/DL G/DL RATIO MG/DL	E SODIUM POTAS CHLORIDE T PROT ALBUMIN GLOBULIN A/G CALCIUM IN PHOS T BILL MHOL/L HMOL/L G/OL G/OL G/OL RATIO MG/OL MG/O	E SODIUM POTAS CHLORIDE T PROT ALBUMIN GLOBULIN A/G CALCIUM IN PHOS T BILLI HIGAL/L HMOL/L G/DL G/DL G/DL G/DL RATIO HG/DL HG/	F: 1 DOSE LEVEL: 0 DOSAGE UNIT: MG/KG 143.4 5.75 104.2 6.6 3.9 2.7 1.44 9.7 5.8 143.9 6.53 106.9 6.8 3.9 2.7 1.44 9.7 5.5 144.9 6.18 10.10.3 6.8 4.0 2.7 1.44 9.7 5.5 1.44 9.7 5.5 1.44 9.7 5.9 1.44 9.7 5.9 1.44 9.7 5.9 1.44 9.7 5.9 1.44 9.7 5.9 1.44 9.7 5.9 1.44 9.7 5.9 1.44 9.7 5.9 1.44 9.7 5.9 1.44 9.7 5.9 1.44 9.7 5.9 1.44 9.7 5.9 1.44 9.7 5.9 1.44 9.7 5.9 1.44 9.7 5.9 1.44 9.7 9.8 5.9 1.44 9.7 9.8 9.8 7.1 4.4 9.7 9.8 9.8 7.1 4.4 9.7 9.8 9.8 7.1 4.4 9.7 9.8 9.8 7.1 4.4 9.7 9.8 9.8 7.1 4.4 9.7 9.8 9.8 7.1 4.4 9.7 9.8 9.8 7.1 4.4 9.7 9.8 9.8 7.9 9.8 1.45 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 9.8 7.9 7.9 7.9 7.9 7.9 7.9 7.9 7.9 7.9 7.9	Harrow Potas	Hardle Sodium Fotas Chloride T Prot Albumin Globulin ArG Calcium In Phos T Bill Higher T Prot Albumin GLobulin ArG Calcium In Phos T Bill Higher Highe	Part SODIUM POTAS CHLORIDE T PROT ALBUMIN GLOBULIN AvG CALCIUM IN PHOS T BIL	SODIUM POTAS CHLORIDE T PROT ALBUMIN GLOBULIN A-G CALCIUM IN PHOS T BILI	Part SODIUM POTAS CHLORIDE T PROT ALBUMIN GLOBULIN AvG CALCIUM IN PHOS T BILLI	Hard SODIUM POTAS CHLORIDE T PROT ALBUMIN GLOBULIN AvG CALCIUM IN PHOS T BILLI	Figure Formation Formati	SODIUM POTAS CHLORIDE T PROT ALBUMIN GLOBULIN AvG CALCIUM IN PHOS T BILLI	Fig. SODIUT POTAS CHLORIDE T PROT ALBUMIN GLOBULIN AvG CALCIUM IN PHOS T BILLI INCL. INCL.	SOUTH POTAS CHLORIDE T PROT ALBUHIN GLOBULIN ANG CALCIUM IN PHOS T BILLI HIGHLY HIGHLY GLOBULIN GLOBULIN ANG CALCIUM IN PHOS T BILLI HIGHLY HIGHLY GLOBULIN GLOBULIN ANG MG/DL HIGHLY HIGHLY GLOBULIN GLO	SODIUM POTAS CHLORIDE T PROT ALBUMIN GLOBULIN ACE CALCIUM IN PHOS T BILLI MOL.1. MOL.1. COD. G.OL. G.OL. G.OL. MOL.1. MG.OL. MG.	SODIUM POTAS CHLORIDE T PROT ALBUMIN GLOBULIN AGE CALCIUM IN PHOS T BILLI HOLL MOLLL MOLLL MOLLL COLL GOLL GOLL GOLL NOLL NOLL MOLLL MOLLL MOLLL COLL GOLL GOLL GOLL NOLL NOLL NOLL MOLL NOLL NOLL GOLL GOLL GOLL NOLL NOLL N	## SODIUM POTAS CHLORIDE T PROT ALBUMIN GLOBULIN ANG CALCIUM IN PHOS T BILLI FROLL HOLL. H

APPENDIX 7
INDIVIDUAL CEINICAL CHEMISTRY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS
WEEK 13 FEMALES

ANIMAL NUMBER	BUN MG/DL	CREAT MG/DL	GLUCOSE MG/DL	T CHOL MG/DL	AST U/L	ALT U/L	AEK P	F 7.
GROUP: 1	DOSE LEVEL:	EL: 0	DOSAGE	DOSAGE UNIT: MG/KG	9			
08382	15	9.	86	29	· 47	19	48	230
08383	15	Ľ.	96	99	80	37	46	381
08384 H1	0	۲.	95	114	69	21	46	241
08385	15	9	97	109	67	24	54	104
08386	15	9.	88	0.6	72	18	40	394
08387 H1	16	۲.	9.0	113	66	21	41	686
08388	15	9.	104	94	82	19	43	459
08389	14	9	93	91	81	22	53	388
08390	14	9.	93	99	57	23	32	158
08391	15	9.	66	109	ĸ	20	49	162
MEAN	14	9.	95	93	23	22	47	311
S.D.	1.9	9 .11	4.6	18.3	13.1	5.5	8.8	155.2
GROUP: 2	DOSE LEVEL:	EL: 100	DOSAGE	DOSAGE UNIT: MG/KG	9			
08422 H1	14	٧.	100	. 82	67	23	81	282
08423 H1	15	۲.	104	85	99	21	52	364
08424 H2	16	9.	98	128	84	53	64	400
08425	16		66	69 .	71	23	53	179
08426	14	`.	68	85	66	56	20	497
08427 H1	13	9	109	118	56	29	09	140
08428	14	9.	101	82	82	38	47	285
08429	12	۲.	105	. 28	2,6	19	96	280
08430	12	4.	66	122	63	20	29	25
08431	14	۰,	92	124	51	18	29	129
MEAN	14	٠.	86		71	25	58	261
S.D.	1.4	•	7.3	22.4	14.9	6.1	21.1	136.4

APPENDIX 7
INDIVIDUAL CLINICAL CHEMISTRY VALUES
SUBCHRONIC TOXICITY STUDY IN RATS
WEEK 13 FEMALES

BUN MG/DL	CREAT MG/DL	GLUCOSE MG/DL	T CHOL	AST U/L	ALT UZL	ALK P	C FDH
) 	1 1 1 1 1 1) 	 	; ; ; ; ;	! ! !	; ; ; ; ;	
DOSE LEVI	EL: 200	394500	UNIT: MG/K	o			
14	9.	0.6	126	58	20	99	225
14	9.	94	115	55	16	41	217
13	9.	68	67	65	22	20	202
16	۲.	77	91	23	24	61	332
15	۲.	159	123.	20	22	46	106
12	9.	110	113	49	24	8Z	236
12	9.	94	105	64	22	46	153
Φ.	9.	83	93	64	27	4	305
12	9.	92	129	80	29	52	295
11	٠.	111	131	99	24	41	155
13	9.	100		99	24	46	223
2.0	. 04	23.4		7.1	3.8	13.2	72.6
DOSE LEVE	il.: 800	DOSAGE	UNIT: MG/K	(1)			
15	۰.	106	122	80	44	39	131
14	9.	104	105	55	18	27	316
=	9.	105	142	09	32	62	119
15	9.	88	123	94	24	23	349
14	9.	96	158	29	20	20	136
15	9.	9.0	124	52	22	51	220
15	ъ.	. 61	117	66	44	84	337
10	9.	81	127	66	25	41	484
11	9.	119	155	96	29	49	. 405
18	9.	9.0	155	53	29	94	101
14	9.	26	133	65	53	49	260
2.4	.03	11.3	18.4	13.2	9.1	18.8	136.2
	BUN MG/DL 14 15 15 16 17 18 19 11 11 11 11 11 11 11 11 11	CAEA MG/D 12 20 20 20 20 20 20 20 20 20 2	CREAT GLU MG/DL MG	CREAT GLU MG/DL MG MG/DL MG 200 .6 .6 .6 .6 .6 .6 .6 .6 .6 .6	CREAT GLUCOSE T CHOL MG/DL MG/DL MG/DL .6 90 126 .6 94 115 .6 94 115 .6 94 115 .6 99 123 .6 99 123 .6 99 123 .6 110 113 .6 100 109 .6 100 100 .6 100 100 .7 100 100 .8 100 1	CREAT GLUCOSE T CHOL AST AL MG/DL MG/DL U/L U/L U/L U/L U/L U/L U/L U/L U/L U/	CREAT GLUCOSE T CHOL AST ALT HG/DL U/L U/L U/L U/L U/L U/L U/L U/L U/L U/

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APPENDIX 8

Individual Animal Summary Report

A** PATH/TOX SYSTEM OUTPUT *** SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88 PAGE: 164

STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: B08362 SEX: MALE DOSE GROUP: 1 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE DATE OF DEATH: 07/14/86 STUDY DAY OF DEATH: 95 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 563.2 GRAMS DATE AND TIME OF NECROPSY: 07/14/86 8:16 PROSECTOR: DOUGLAS HERNOON POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, OUM, PHD, DACUP ABSOLUTE ORGAN WEIGHT RELATIVE ORGAN TO BRAIN O R G A N	n	! ! !
ANIMAL NUMBER: B08362 SEX: MALE DOSE GROUP: 1 SACRIFICE STATUS: SCHEDULED, TERMINAL BODY WE DATE OF DEATH: 14 TERMINAL BODY WE DATE OF DEATH: 14 TERMINAL BODY WE DATE OF DEATH: 17/14/86 8:16 PROSECTOR: DOUGLAS HERNOON PROCOPER: SI POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, OUM, PHD, DACUP WEIGHER: DOUBLER: DOUBLAS WEIGHT RELATIVE ORGAN TO BRAIN	NAL SACRIFICE LIGHT: 563.2 GRAMS ID JONES, OUM, PHD, DACUS	GLAS HERNDON
ANIMAL NUMBER: B08362 SEX: MALE BOSE GROUP: 1 SACRIFICE STATUS DATE OF DEATH: 07/14/86 STUDY DAY OF DEATH: 95 STUDY WEEK OF DEATH: 14 DATE AND TIME OF NECROPSY: 07/14/86 8:16 PROSECTOR: DOUGLAS HERNOON POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, OUM, PHD, DACU-	S: SCHEDULED, TERMI TERMINAL BODY WE RECORDER: SI	JP WEIGHER: DOI
ANIMAL NUMBER: B08362 SEX: MALE DOSE GROUP: 1 DATE OF DEATH: 07/14/86 STUDY DAY OF DEATH: 95 STUDY WEEL DATE AND TIME OF NECROPSY: 07/14/86 8:16 PROSECTOR: DOUGLAS POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JOH ABSOLUTE ORGAN WEIGHT ORGAN WE	SACRIFICE STATUS K OF DEATH: 14 HEDNOON	NES, OVM, PHD, DACK
ANIMAL NUMBER: B08362 SEX: MALE DATE OF DEATH: 07/14/86 STUDY DAY OF DEATH DATE AND TIME OF NECROPSY: 07/14/86 8:16 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL ABSOLUTE ORGAN	DOSE GRO 95 POSECTOR	ATHOLOGIST: SID JO WEIGHT ORGAN WE
ANIMAL NUMBER: B08362 DATE OF DEATH: 07/14/86 DATE AND TIME OF NECROPSY: POST-FIX WEIGHER: NOT REQUI	SEX: MALE STUDY DAY OF DEATH	RED BY PROTOCOL
	ANIMAL NUMBER: B08362 DATE OF DEATH: 07/14/86	DAIE AND LINE OF NECKOFST: POST-FIX WEIGHER: NOT REQUI

DNEY (KD): -NEPHROPATHY, CHRONIC PROGRESSIVE,-	KIDNEY (KD):	GENERAL INFORMATION (XX):	GENERAL INFO	-АРРЕАКЕО NORMAL
ніѕторатнососу	S	HOLOGY OBSERUATIONS NECROPSY	1	CLINICAL OBSERVATIONS
WEIGHT TAKEN	2.466	% 226°	5.50	TEST15/EP1010 (TP)
WEIGHT TAKEN	6.206	2.457 %	13.84	L10ER (L1)
MEIGHT TAKEN	1.578	.625 %	3.52	KIDNEY (KD)
WEIGHT TAKEN	. 368	.146 %	.82	SPLEEN (SP)
WEIGHT TAKEN	.740	.293 %	1.65	HEART (HT)
WEIGHT TAKEN	1.000	% 96£.	2.23	BRAIN W/STEM (BR)
WEIGHT TAKEN	. 0206	.0082 %	. 046	ADRENAL (AD)
*******	1 1 1 1 1 1 1 1	1 1 1 1 1	!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!	
STATUS	WEIGHT RATIO	TO BODY WEIGHT (%)	(GRAMS)	ORGAN NAME
	ORGAN TO BRAIN	ORGAN WEIGHT RELATIVE 0	ABSOLUTE ORGAN WEIGHT	•

MINIMAL
LIUER (LI):
-FOCI OF MONONUCLEAR CELLS,-MINIMAL
LUNG (LU):
-PERIBRONCHIAL/PERIVASCULAR,
INFILTRATION, LYMPHOID,-SLIGHT

APPENDIX B *** PATH/TOX SYSTEM OUTPUT *** SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

RECORDER: SID JONES, DUM, PHD, DACUP WEIGHER: DOUGLAS HERNDON 563.2 GRAMS SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE TERMINAL BODY WEIGHT: PATHOLOGIST: SID JONES, DUM, PHD, DACUP STUDY WEEK OF DEATH: 14 PROSECTOR: DOUGLAS HERNDON DOSE GROUP: 1 STUDY DAY OF DEATH: 95 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL DATE AND TIME OF NECROPSY: 07/14/86 8:16 SEX: MALE DATE OF DEATH: 07/14/86 NUMBER: 808362 ANIMAL

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AD), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN WASTEM (BR), CECUM (CE), COLON (CD), CORD, CERUICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUDDENUM (DU), EPIDIDYHIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIONEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERUE, SCIATIC (SN), PANCREAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR),
URINARY BLADDER (UB), ACOLLECTED/TAKEN (XW)

FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AD), BONE, FEMUR (FE), BONE, STERNUM (SB),

BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORO, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),

DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), LACRIMAL GL, EXO

LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM),

NERUE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SU)

SKIN (SK), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY),

TRACHEA (TR), URINARY BLADDER (UB) 뿔

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

*** PATH/TOX SYSTEM OUTPUT *** SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88 PAGE: 166

STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

DULED, TERMINAL SACRIFICE INAL BODY WEIGHT: 452.7 GRAMS RECORDER: SID JONES, DUM, PHD, DACUP WEIGHER: BARBARA DAY	0 R G A N S T A T U S	WEIGHT TAKEN	НІЅТОРАТНОLOGY	FLAMMATION, HARDERIAN SLAN ATHY, DEGENERATIVE,-MINIMA TITIS,-MINIMAL IAL/PERIVASCULAR,
SCHE	ORGAN TO BRAIN WEIGHT RATIO	1,000 1,000 .650 .335 1,374 5,268	S Z O .	EYE (EY): -CHRONIC IN SLIGHT -CARDIOMYOPY
DOSE GROUP: 1 SACRIFICE STATUS: 195 STUDY WEEK OF DEATH: 14 PROSECTOR: BARBARA DAY PHD, DACUP	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	.0137 % .463 % .301 % .155 % .636 % 2.439 %	HOLOGY OBSERUATI NECROPSY	GENERAL INFORMATION (XX): >NOTE:>EXTERNAL OBSERVATIONS:NONE
. ОЕАТН	ABSOLUTE ORGAN WEIGHT (GRAMS)	2.10 2.10 1.36 2.88 11.04 4.92	⊥	GENERAL INF
ANIMAL NUMBER: B08363 SEX: MALE DATE OF DEATH: 07/14/86 STUDY DAY OF DATE AND TIME OF NECROPSY: 07/14/86 10:53 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL	ORGAN NAME	ADRENAL (AD) BRAIN W-STEM (BR) HEART (HT) SPLEEN (SP) KIDNEY (KD) LIUER (LI) TESTIS/EPIDID (TP)	CLINICAL OBSERVATIONS	- APPEARED NORMAL

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/IOX SYSTEM OUTPUT *** APPENDIX 8

PRINTED: 12-MAY-88 PAGE: 167

STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

TERMINAL BODY WEIGHT: 452.7 GRAMS RECORDER: SID JONES, DUM, PMD, DACUP SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE WEIGHER: BARBARA DAY PATHOLOGIST: SID JONES, DUM, PHD, DACUP STUDY WEEK OF DEATH: 14 PROSECTOR: BARBARA DAY DOSE GROUP: 1 DATE OF DEATH: 07/14/86 STUDY DAY OF DEATH: 95
DATE AND TIME OF NECROPSY: 07/14/86 10:53 PROSE POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL SEX: MALE ANIMAL NUMBER: B08363

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (CAN), AORTA, THORACIC (AD), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRENAL, CORTEX (AC), ADRENAL, MEDULLA (CO), CORD, CORD, LUMBAR (LC), CORD, THORACIC (TC),
BRODENUM (CO), EDIDYMIS (EP), ESCHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
HAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR),
URINARY BLADDER (UB), ^COLLECTED/TAKEN (XW) THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRTA, THORACIC (AD), BONE, FEMUR (FE), BONE, STERNUM (SB),

BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORO, CERVICAL (CS), CORO, LUMBAR (LC), CORO, THORACIC (TC),

BUODENUM (DU), EPIDIOYMIS (EP), ESOPHAGUS (ES), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXO (EO),

LN, MESENTERIC (MS), MANMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM),

NERUE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SU),

SKIN (SK), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), RACHEA (TR), URINARY BLADDER (UB)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

*** PATH/TOX SYSTEM OUTPUT *** SUBCHRONIC TOXICITY STUDY IN RATS

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INDIVIDUAL ANIMAL SUMMARY REPORT

001	2399108
100	NUMBER:
	STUDY

DATE AND TIME OF NECROPSY: 02/14/86 13:21 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL		: 95 STUDY WEEK OF DEATH: 14 PROSECTOR: DQUGLAS HERNDON PATHOLOGIST: SID JONES, OUM, PHD, DACUP	2	NDON RECORDER: 542.2 GRANS NDON RECORDER: SID JONES, DVM, PHD, DACUP , DUM, PHD, DACUP WEIGHER: DOUGLAS HERNDON
ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (*)	ORGAN TO BRAIN WEIGHT RATIO	ORGAN STATUS
ADRENAL (AD) BRAIN W.STEM (BR)		387 %	. 0244	i ' ' '
	1.07 3.04	.278 % .196 % .559 %	.507 .507 1.445	
LIVER (LI) TESTIS/EPIDID (TP)	14.17 5.83	2.609 % 1.072 %	6.743 2.772	WEIGHT TAKEN WEIGHT TAKEN
CLINICAL OBSERVATIONS	! -	OLOGY OBSERUATI	S Z O I	HISTOPATHOLOGY
-APPEARED NORMAL	GENERAL INFO	NERAL INFORMATION (XX); NOTE;>EXTERNAL OBSERVATIONS:NONE	BONE, FEMUR (FE): -ARTICULAR SURFACE NI HEART (HT): -CARDIOMYOPATHY, DEGI LACRIMAL GL, EXO (EO) -FOCAL MONONUCLEAR II LUNG (LU): -PERIBRONCHIAL/PERIV	BONE, FEMUR (FE): HEART (HT): -CARDIOMYOPATHY, DEGENERATIVE, -MINIMAL LACRIMAL GL, EXO (EQ): -FOCAL MONONUCLEAR INFILTRATE, -SLIGHT LUNG (LU): -PERIBRONCHIAL/PERIVASCULAR, INFILTRATION, LYMPHOID, -MINIMAL

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/TOX SYSTEM OUTPUT *** APPENDIX 8

PRINTED: 12-MAY-88

STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

RECORDER: SID JONES, DUM, PHD, DACUP 543.3 GRAMS SACRIFICE WEIGHER: DOUGLAS HERNDON TERMINAL BODY WEIGHT: SACRIFICE STATUS: SCHEDULED, TERMINAL PATHOLOGIST: SID JONES, DUM, PHD, DACUP STUDY WEEK OF DEATH: 14 PROSECTOR: DOUGLAS HERNDON DOSE GROUP: 1 OF DEATH: 07/14/86 STUDY DAY OF DEATH: 95 AND TIME OF NECROPSY: 07/14/86 13:21 PROSE POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL SEX: MALE DATE OF DEATH: 07/14/86 ANIMAL NUMBER: B08364

DATE

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AN), AGRIA, THORACIC (AD), BONE, FEMUR (FE), BONE, STERNUM (SB),

BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),

DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),

LACRIMAL GL, EXD (ED), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG),

MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA),

PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS),

SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR),

URINARY BLADDER (UB), ^COLLECTED/TAKEN (XW)

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AH), ADRIA, THORACIC (AD), BONE, STERNUM (SB), BRAIN W-STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC), DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LIVER (LI), LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SPLEEN (SP), STOMACH, GL (ST), STOMACH, GL (ST), URINARY BLADOER (UB) FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: 뿔

*** ALL ORGANS/IISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

A** PATH/TOX SYSTEM OUTPUT *** SUBCHRONIC TOXICITY STUDY IN RATS

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STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

OSE GROUP: 1 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE 5 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 605.9 GRAMS SECTOR: TIM GROVE HOLOGIST: SID JONES, DVM, PHD, DACUP WEIGHER: TIM GROVE	ORGAN Status
SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE F DEATH: 14 TERMINAL BODY WEIGHT: 605.9 RECORDER: SID JONES, DVM, , DVM, PHD, DACUP WEIGHER: TIM GROVE	DRGAN TO BRAIN WEIGHT RATIO
DOSE GROUP: 1 SACRIFICE STATUS: 95 STUDY WEEK OF DEATH: 14 PROSECTOR: TIM GROUE PATHOLOGIST: SID JONES, DUM, PHD, DACUP	ORGAN WEIGHT RELATIVE O
SEX: MALE DOSE GROUP: 1 STUDY DAY OF DEATH: 95 STUDY WEEK 14/86 14:42 PROSECTOR: TIM GROVE BY PROTOCOL PATHOLOGIST: SID JOW	ABSOLUTE ORGAN WEIGHT (GRAMS)
ANIMAL NUMBER: B08365 SEX: MALE DATE OF DEATH: 07/14/86 STUDY DAY OF DATE AND TIME OF NECROPSY: 07/14/86 14:42 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL	ABSOLUTE ORGAN WE (GRAMS)

ORGAN NAME	(GRAMS)	TO BODY WEIGHT (%)	WEIGHT RATIO	STATUS
	f = # +	** ** ** ** **	1 1 1 1 1 1	111111
ADRENAL (AD)	.053	% 8800°	.0277	WEIGHT TAKEN
BRAIN W/STEM (BR)	1.93	.318 %	1.000	WEIGHT TAKEN
HEART (HT)	1.50	.247 .%	777.	WEIGHT TAKEN
SPLEEN (SP)	00.	.132 %	. 414	WEIGHT TAKEN
KIDNEY (KD)	3.82	.631 %	1.983	WEIGHT TAKEN
LIVER (LI)	14.97	2.471 %	7,767	WEIGHT TAKEN
TESTIS/EPIDID (TP)	5.34	.881 %	2.770	WEIGHT TAKEN
CL INICAL OBSERVATIONS	PATHOL	HOLOGY OBSERUATIONS NECROPSY	SNO	HISTOPATHOLOGY
-APPEARED NORMAL	 - - - - -	GENERAL INFORMATION (XX):	ADREMAL, CORTEX (AC) :	TEX (AC) :

EYE (EY) : -CHRONIC INFLAMMATION, HARDERIAN GLAND,--UACUOLIZATION, - SLIGHT >NOTE:>EXTERNAL OBSERVATIONS:NONE

MINIMAL
LUNG (LU):
-PERIBRONCHIAL/PERIVASCULAR,
INFILTRATION, LYMPHOID,-SLIGHT
PANCREAS (PA):
-INFLAMMATION, CHRONIC,-SLIGHT

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/TOX SYSTEM DUTPUT *** APPENDIX B

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STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE PATHOLOGIST: SID JONES, DUM, PHD, DACUP STUDY WEEK OF DEATH: 14 PROSECTOR: TIM GROVE DOSE GROUP: 1 STUDY DAY OF DEATH: 95 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL DATE OF DEATH: 02/14/86 STUDY DAY OF DATE AND TIME OF NECROPSY: 02/14/86 14:42 SEX: MALE ANIMAL NUMBER: B08365

TERMINAL BODY WEIGHT: 605.9 GRAMS RECORDER: SID JONES, DUM, PHD, DACUP WEIGHER: TIM GROVE

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AD), BONE, FEMUR (FE), BONE, STERNUM (SB),

BRAIN W-STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),

BRAIN W-STEM (BR), CECUM (CE), KIDNEY (KD),

BRAIN (BL), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),

LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG),

MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA),

PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS),

SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR),

URINARY BLADDER (UB), ^COLLECTED/TAKEN (XW)

ADRENOL, MEDULLA GM), GONTA, THORACIC (GD), BONE, FEMUR (FE), BONE, STERNUM (SB), BRAIN W/STEM (BR), CECUM (CE), ADRENOL, MEDULLA GM), EPIDIDYMIS (EP), CORD, MANNISCIE, CARD, MANNISCIE, SKELETAL (SM), NESENTERIC (MS), MAND GAID, MAND SALIVARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL UESICLE (SU), SKIN (SK), SPLEEN (SP), STOMACH, GL (ST), TRACHEA (TR), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR), FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: URINARY BLADDER (UB) 포

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

SUBCHRONIC TOXICITY STUDY IN RATS APPENDIX B *** PATH/TOX SYSTEM OUTPUT ***

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STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DF DEATH: 14 TERMINAL BODY WEIGHT: 457.0 GRAMS
Y
RECORDER: SID JONES, DUM, PHD, DACUP
S, DUM, PHO, DACUP WEIGHER: BARBARA DAY DOSE GROUP: 1 SACRIFICE STATUS: 4: 95 STUDY WEEK OF DEATH: 14 PROSECTOR: BARBARA DAY PATHOLOGIST: SID JONES, DVM, PHD, DACUP DATE OF DEATH: 02/14/86 STUDY DAY OF DEATH: 95
DATE AND TIME OF NECROPSY: 02/14/86 15:07 PROSE
POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL. PATHO SEX: MALE ANIMAL NUMBER: 808366

ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN MEIGHT RATIO	ORGAN STATUS
		5 67 60	0000	NAME TO STATE
BRAIN W/STEM (BR)	2.05	. 448	1.000	WEIGHT TAKEN
HEART (HT)	1.28	.279 %	.623	WEIGHT TAKEN
SPLEEN (SP)	.84	.184 %	.411	WEIGHT TAKEN
KIDNEY (KD)	3.28	. 718 ×	1.601	WEIGHT TAKEN
LIVER (LI)	12.41	2.716 %	6.058	WEIGHT TAKEN
TESTIS/EP1010 (TP)	5.17	1.130 %	2.521	WEIGHT TAKEN
CLINICAL OBSERVATIONS	PATHOL	HOLOGY OBSERUATIONS NECROPSY	S Z O	HISTOPATHOLOGY
-APPEARED NORMAL	GENERAL INFORMATION	GENERAL INFORMATION (XX): VALUE OF TERMS DESCRIPTIONS NOWE	ADRENAL, CO	ADRENAL, CORTEX (AC):

EYE (EY):

-CHRONIC INFLAMMATION, HARDERIAN GLAND,-SLIGHT

KIDNEY (KD); -NEPHROPATHY, CHRONIC PROGRESSIVE,-SL IGHT

LIVER (LI) : -BILE DUCT, INFLAMMATION, CHRONIC,-

CUNG (LIJ) : MINIMAL

INFILTRATION, LYMPHOID, -SLIGHT PARATHYROID (PT): -PERIBRONCHIAL/PERIUASCULAR,

>SECTION EXAMINED; TISSUE NOT PRESENT

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/TOX SYSTEM CUTPUT *** APPENDIX B

PRINTED: 12-MAY-88

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

457.0 GRAMS SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE WEIGHER: BARBARA DAY TERMINAL BODY WEIGHT: PATHOLOGIST: SID JONES, DUM, PHD, DACUP STUDY WEEK OF DEATH: 14 PROSECTOR: BARBARA DAY DOSE GROUP: 1 STUDY DAY OF DEATH: 95 DATE AND TIME OF NECROPSY: 07/14/86 15:07 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL SEX: MALE DATE OF DEATH: 07/14/86 ANIMAL NUMBER: B08366

RECORDER: SID JONES, DUM, PHD, DACUP

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRTA, THDRACIC (AD), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W.STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
BUDDENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUMG (LU), MAMMARY GLAND (MG),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SU), SKIN (SK), SKIN, OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR),
URINARY BLADDER (UB), CCOLLECTED/TAKEN (XW) THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, MEDULLA (AM), AORTA, THORACIC (AD), BONE, FEMUR (FE), BONE, STERNUM (SB), BRAIN WASTEM (BR), CECUM (CE),
COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC), DUDDENUM (DU), EPIDIOYMIS (EP),
ESOPHAGUS (ES), HEART (HT), ILEUM (IL), JEJUNUM (JE), LACRIMAL GL, EXO (EO), LN, MESENTERIC (MS), MANMARY GLAND (MG),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA),
PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SPLEEN (SP), STOMACH, GL (ST),
STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB) 뿔

*** PATH/TOX SYSTEM OUTPUT *** SUBCHRONIC TOXICITY STUDY IN RATS

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INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

TERMINAL BODY WEIGHT: 451.7 GRAMS
RECORDER: SID JONES, DUM, PHD, DACUP
WEIGHER: NOT REQUIRED BY PROTOCOL SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE H: 95 STUDY WEEK OF DEATH: 14 PROSECTOR: DOUGLAS HERNDON PATHOLOGIST: SID JONES, DVM, PHD, DACUP DOSE GROUP: 1 DATE OF DEATH: 07/14/86 STUDY DAY OF DEATH: 95
DATE AND TIME OF NECROPSY: 07/14/86 9:10 PROSE
POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL PATHO SEX: MALE ANIMAL NUMBER: 808367 DATE OF DEATH: 07/14/86

*** ANIMAL HAS NO DRGAN WEIGHTS RECORDED ***

-RIGHT

CLINICAL OBSERVATIONS	THOLOGY OBSERVATI NECROPSY	HISTOPATHOLOGY
EYE-CHROMODACRYORRHEA	EYE (EY): -GLOBE RUPTURED POST MORTEM; LEFT -GOLLECTED/TAKEN (XW): -ELECTRON MICROSCOPY SAMPLE; LIVER GENERAL INFORMATION (XX): >NOTE:>EXTERNAL OBSERVATIONS:RIGHT EYE- CHROMODACRYORRHEA	EYE (EY): JUMBEMARKABLE LIVER (LI): -BILE DUCT, INFLAMMATION, CHRONIC,- MINIMAL LUNG (LU): -PERIBRONCHIAL/PERIVASCULAR, INFILTRATION, LYMPHOID,-SLIGHT PARATHYROID (PT): >SECTION EXAMINED; TISSUE NOT PRESENT

APPENDIX 8 *** PATH/TOX SYSTEM QUIPUT *** SUBCHRONIC TOXICITY STUDY IN RATS

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INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

TERMINAL BODY WEIGHT: 451.7 GRAMS RECORDER: SID JONES, DUM, PHD, DACUP WEIGHER: NOT REQUIRED BY PROTOCOL 451.7 GRAMS SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE PATHOLOGIST: SID JONES, DUM, PHD, DACUP STUDY WEEK OF DEATH: 14 PROSECTOR: DOUGLAS HERNDON DOSE GROUP: 1 OF DEATH: 07/14/86 STUDY DAY OF DEATH: 95 AND TIME OF NECROPSY: 07/14/86 9:10 PROSE POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL SEX: MALE DATE OF DEATH: 07/14/86 DATE AND TIME OF NETRANS ANIMAL NUMBER: B08367

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AD), BONE, FEMUR (FE), BONE, STERNLM (SB),
BRAIN WASTEM (GR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
BUODENUM/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), LEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXO (EO),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GL (SG),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI),
PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST),
STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), TRACHEA (TR), URINARY BLADDER (UB) THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AD), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W.STEM (BR), CECUM (CE), CORO, CORO, CORO, LUMBAR (LC), CORO, THORACIC (TC),
DUDDENUM (DU), EPIDIDYNIS (EP), ESOPHAGUS (ES), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXD (ED)
, LN, MESENTERIC (MS), HAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM),
NERUE, SCIATIC (SN), PANCREAS (PA), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SU), SKIN (SK),
SPLEEN (SP), STOMACH, GL (SI), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR), THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: URINARY BLADDER (UB)

*** PATH/IOX SYSTEM OUTPUT *** SUBCHRONIC TOXICITY STUDY IN RATS

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STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: B08368 SEX: MALE DATE OF DEATH: 07/15/86 STUDY DAY OF DATE AND TIME OF NECROPSY: 07/15/86 8:08 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL	DEATH:	WEEK O	SCHE	SCHEDULED, TERMINAL SACRIFICE TERMINAL BODY WEIGHT: 511.3 GRAMS RECORDER: SID JONES, OUM, PHD, DACUP WEIGHER: DOUGLAS HERNDON
ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO	ORGAN Status
ADRENAL (AD) BRAIN W/STEM (BR) HEART (HT)	2.04	. 0136 % . 399 % . 275 %	1.000	
SPLEEN (SP) KIDNEY (KD) LIUER (LI) TESTIS/EPIDID (TP)	.02 3.19 13.00 5.73	. 121 % . 624 % 2.543 % 1.120 %	1.562 6.368 2.804	WEIGHT TAKEN WEIGHT TAKEN WEIGHT TAKEN WEIGHT TAKEN
CLINICAL OBSERVATIONS	١.	HOLOGY OBSERUATIONS NECROPSY	S Z O	HISTOPATHOLOGY
-APPEARED NORMAL	GENERAL INFO	GENERAL INFORMATION (XX): >NOTE:>EXTERNAL OBSERVATIONS:NONE	EYE (EY): -CHRONIC INF SLIGHT SLIGHT -PERIBRONCHI INFILTRATIO	E (EY): -CHRONIC INFLAMMATION, HARDERIAN GLAND,- SLIGHT NG (LU): -PERIBRONCHIAL/PERIVASCULAR, INFILTRATION, LYMPHOID,-SLIGHT

APPENDIX 8 *** PATH/TOX SYSTEM OUTPUT *** SUBCHRONIC TOXICITY STUDY IN RATS

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INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

RECORDER: SID JONES, DUM, PHD, DACUP WEIGHER: DOUGLAS HERNDON 511.3 GRAMS DUP: 1 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 511.3 TERMINAL BODY WEIGHT: RECORDER: SID JONE: PATHOLOGIST: SID JONES, DUM, PHD, DACUP PROSECTOR: DOUGLAS HERNDON DOSE GROUP: 1 DEATH: 96 STUDY DAY OF POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL AND TIME OF NECROPSY: 07/15/86 8:08 SEX: MALE DATE OF DEATH: 07/15/86 ANIMAL NUMBER: B08368 DATE

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AD), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W.STEM (BR), CECUM (CC), CORD, CORD, CERUICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUDDENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERUE, SCIATIC (SN), PANCREAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SU), SKIN (SK), SKIN, OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR),
URINARY BLADDER (UB), ^COLLECTED/TAKEN (XW) THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:
ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (OU), EPIDIDYMIS (EP), ESOPHAGUS (ES), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXO (EO)
, LIVER (LI), LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB) 뿔

APPENDIX 8 *** PATH/TOX SYSTEM OUTPUT *** SUBCHRONIC TOXICITY STUDY IN RATS

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INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

ANIMAL NUMBER: B08369 SEX: MALE DATE OF DEATH: 07/15/86 STUDY DAY OF DATE AND TIME OF NECROPSY: 07/15/86 10:00 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL	DEATH: 9.	· WEEK O GROUE D JONES	SCHEDULED, TER TERMINAL BODY RECORDER: WEIGHER: I	RMINAL SACRIFICE WEIGHT: 508.4 GRAMS SID JONES, DUM, PHD, DACUP TIM GROUE
ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO	SULATO
ADRENAL (AD) BRAIN W/STEM (BR) HEART (HT) SPLEEN (SP) KIDNEY (KD) LIUER (LI) TESTIS/EPIDID (TP)				MEIGHT TAKEN
CLINICAL OBSERVATIONS	H	OLOGY OBSERUATE NECROPSY	SVO	HISTOPATHOLOGY
-APPEARED NORMAL	GENERAL INFO	E:>EXTERNAL OBSERUATIONS:NONE	EYE (EY): -CHRONIC INFLAMMATII SLIGHT HEART (HT): -CARDIOMYOPATHY, DE KIDNEY (KD): -NEPHROPATHY, CHRON MINIMAL -TUBULE, MICROCONCRI LUNG (LU): -PERIBRONCHIAL/PERI INFILITRATION, LYMP MAMMARY GLAND (MG): ->SECTION EXAMINED: -INFLAMMATION, CHRO PARATHYROIO (PT): ->SECTION EXAMINED: -NELAMMATION, CHRO PARATHYROIO (PT):	CE (EY): -CHRONIC INFLAMMATION, HARDERIAN GLAND,- SLIGHT -CARDIOMYOPATHY, DEGENERATIVE,-MINIMAL -CARDIOMYOPATHY, DEGENERATIVE,-MINIMAL -TUBULE, MICROCONCRETION,-SLIGHT
1 1 1 1 1 1 1	1 1 1 1 1 1 1		1	f t t t t t t t t t t t t t t t t t t t

APPENDIX 8 *** PATH/IDX SYSTEM OUTPUT *** SUBCHRONIC TOXICITY STUDY IN RATS

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INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

TERMINAL BODY WEIGHT: 508.4 GRAMS RECORDER: SID JONES, DUM, PHD, DACUP SACRIFICE WEIGHER: TIM GROVE SACRIFICE STATUS: SCHEDULED, TERMINAL PATHOLOGIST: SID JONES, DUM, PHD, DACUP STUDY WEEK OF DEATH: 14 PROSECTOR: TIM GROUE DOSE GROUP: 1 STUDY DAY OF DEATH: 96 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL AND TIME OF NECROPSY: 07/15/86 10:00 DATE OF DEATH: 07/15/86 ANIMAL NUMBER: B08369 DATE

DUGDENAL, CORTEX (AC), ADREMAL, MEDULLA (AM), AORTA, THORACIC (AD), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W.STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
BUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR),
URINARY BLADDER (UB), ^COLLECTED/TAKEN (XW) THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB), BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC), DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), ILEUM (IL), JEJUNUM (JE), LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TM), TRACHEA (TR), URINARY BLADDER (UB) FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

*** PATH/TOX SYSTEM DUTPUT *** SUBCHRONIC TOXICITY STUDY IN RATS

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STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

SCHEDULED, TERMINAL SACRIFICE TERMINAL BODY WEIGHT: 459,9 GRAMS RECORDER: SID JONES, DUM, PHD, DACUP WEIGHER: TIM GROVE	ORGAN STATUS	MEIGHT TAKEN
	ORGAN TO BRAIN WEIGHT RATIO	
- U	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	
SEX: MALE DOSE GROUP: 1 STUDY DAY OF DEATH: 96 STUDY WEEK 15/86 13:59 PROSECTOR: TIM GROVE BY PROTOCOL PATHOLOGIST: SID JONE	ABSOLUTE ORGAN WEIGHT (GRAMS)	
ANIMAL NUMBER: 808370 SEX: MALE DOSE 1 DATE OF DEATH: 87.15.486 STUDY DAY OF DEATH: 96 DATE AND TIME OF NECROPSY: 87.15.486 13:59 PROSECTI POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL PATHOLO	ORGAN NAME	ADRENAL (AD) BRAIN W/STEM (BR) HEART (HT) SPLEEN (SP) KIDNEY (KD) LIVER (LI) TESTIS/EPIDID (TP)

CHOITE GRAND IN TO	PATHOLOGY, OBSERVATIONS NETPOSSY	HISTORGINGS
	10 OVER 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	
-APPEARED NORMAL	KIDNEY (KD) :	EYE (EY) :
	-PELVIS, DILATED; LEFT, SLIGHTLY	-ONE EXAMINED, -PRESENT
	-H-PELUIS, DILATED; RIGHT, SLIGHTLY.	KIDNEY (KD) :
	GENERAL INFORMATION (XX):	-NEPHROPATHY, CHRONIC PROGRESSIVE,-
	VNOTE: VEXTERNAL OBSERVATIONS: NOWE	MINIMAL
		-PELVIS, DILATATION,-SLIGHT
		LUNG (LU):
		-PERIBRONCHIAL/PERIVASCULAR,
		INFILTRATION, LYMPHOID, -SLIGHT
		PARATHYROID (PT):
		SECTION EXAMINED; TISSUE NOT PRESENT

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/TOX SYSTEM OUTPUT *** APPENDIX 8

PRINTED: 12-MAY-83

INDIVIDIJAL ANIMAL SUMMARY REPORT

STIJDY NUMBER: 2399108

TERMINAL BODY WEIGHT: 459.9 GRAMS RECORDER: SID JONES, DUM, PHD, DACUP SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE WEIGHER: 11M GROVE PATHOLOGIST: SID JONES, DUM, PHD, DACUP STUDY WEEK OF DEATH: 14 PROSECTOR: TIM GROVE DOSE GROUP: 1 DEATH: 96 STUDY DAY OF POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL DATE AND TIME OF NECROPSY: 07/15/86 13:59 SEX: MALE DATE OF DEATH: 07/15/86 ANIMAL NUMBER: B08370

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AG), BONE, FEMUR (FE), BONE, STERNUM (SB),

BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),

BRAIN WASTEM (BR), CECUM (CE), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), LACRIMAL GL, EXO (EO),

LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GL (SG),

MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI),

PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST),

STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), ACOLLECTEDATAKEN (XM)

DOBENDAL, CORTECT CONTROLL CONTROLLE (AM), ADRIA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),

RADENAL, CORTECT CONTROLL (CD), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),

BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), LORD, LUMBAR (LC), LACRIMAL GL, EXO (EO),

DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), HEART (HT), ILEUM (IL), JEJUNUM (JE), LACRIMAL GE), MUSCLE, SKELETAL (SM),

LIVER (LI), LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM),

NERUE, SCIATIC (SN), PANCREAS (PA), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SU), SKIN (SK),

SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMLS (TH), THYROID (TY), TRACHEA (TR), FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: URINARY BLADDER (UB) 포

A** PATH/TOX SYSTEM OUTPUT *** SUBCHRONIC TOXICITY STUDY IN RATS

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STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

DATE AND TIME OF NECROPSY: 07/15/86 15:13 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL	J	PROSECTOR: 11M GROVE PATHOLOGIST: SID JONES, DVM, PHD, DACVP		RECURDER: SID JUNES, DOFT, FAD, DALOF WEIGHER: TIM GROVE
ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO	ORGAN STATUS
1 2 2	1.93	. K	. 0264 1,000 . 715	
SPLEEN (SP) KIDNEY (KD) LIVER (LI) TESTIS/EPIDID (TP)	1.17 3.45 13.44 5.17	.23/ % .699 % 2.722 % 1.047 %	. 600 1.788 6.964 2.679	WEIGHT TAKEN WEIGHT TAKEN WEIGHT TAKEN
CLINICAL OBSERVATIONS	H	OLOGY OBSERUATION NECROPSY	S	HISTOPATHOLOGY
-LEFT EYE-CHROMODACRYORRHEA; MALOCCLUSION	GENERAL	NERAL INFORMATION (XX) : NOTE:>EXTERNAL OBSERVATIONS:LEFT EYE- CHROMODACRYORRHEA, MALOCCLUSION	:	E (EY): -CHRONIC INFLAMMATION, HARDERIAN GLAND,-SLIGHT ART (HT): -CARDIOMYOPATHY, DEGENERATIVE,-MINIMAL VER (LI): -FOCI OF MONDUCLEAR CELLS,-MINIMAL -BILE DUCT, INFLAMMATION, CHRONIC,- MINIMAL NG (LU): -PERIBRONCHIAL/PERIVASCULAR, -NFILTRATION, LYMPHOID,-SLIGHT RATHYROID (PT): -SECTION EXAMINED; TISSUE NOT PRESENT

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/TOX SYSTEM OUTPUT *** APPENDIX 8

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INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

TERMINAL BODY WEIGHT: 493.7 GRAMS RECORDER: SID JONES, DUM, PHD, DACUP SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE WEIGHER: TIM GROVE PATHOLOGIST: SID JONES, DUM, PHD, DACUP STUDY WEEK OF DEATH: 14 PROSECTOR: TIM GRIDUE DOSE GROUP: 1 STUDY DAY OF DEATH: 96 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL DATE AND TIME OF NECROPSY: 07/15/86 15:13 DATE OF DEATH: 07/15/86 ANIMAL NUMBER: B08371

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),

BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),

DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),

LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG),

MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA),

PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS),

SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR),

URINARY BLADDER (UB), ^COLLECTED/TAKEN (XW)

FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BCNE, FEMUR (FE), BONE, STERNUM (SB),

BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),

DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), ILEUM (IL), JEJUHUM (JE), KIDNEY (KD), LACRIMAL GL, EXO (EO),

LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM),

NERUE, SCIATIC (SN), PANCREAS (PA), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL UESICLE (SU), SKIN (SK),

SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB) THE

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/TOX SYSTEM OUTPUT *** APPENDIX B

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INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

GUP: 1 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 487.8 GRAMS: DOWIGLAS HERNDON RECORDER: SID JONES, DUM, PHD, DACUP WEIGHER: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DACUP PROSECTOR: DOUGLAS HERNDON DOSE GROUP: 1 STUDY DAY OF DEATH: 96 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL AND TIME OF NECROPSY: 07/15/86 8:32 SEX: MALE DATE OF DEATH: 07/15/86 ANIMAL NUMBER: 808372

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

CLINICAL DBSERVATIONS

-APPEARED NORMAL

OBSERUATIONS NECROPSY PATHOLOGY

-ELECTRON MICROSCOPY SAMPLE; LIVER COLLECTED/TAKEN (XW) :

>NOTE:>EXTERNAL OBSERVATIONS:NONE GENERAL INFORMATION (XX):

-NEPHROPATHY, CHRONIC PROGRESSIVE,-KIDNEY (KD) : LUMB (LU) : MINIMAL

HISTOPATHOLOGY

-PERIBRONCHIAL/PERIUASCULAR,

>SECTION EXAMINED; TISSUE NOT PRESENT INFILTRATION, LYMPHOID, -SLIGHT PARATHYROID (PT) :

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/TOX SYSTEM OUTPUT *** APPENDIX B

PRINTED: 12-MAY-88

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

TERMINAL BODY WEIGHT: 487.8 GRAMS
RECORDER: SID JONES, DVB, PHD, DACVP
WEIGHER: NOT REQUIRED BY PROTOCOL DUP: 1 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 487.8 PATHOLOGIST: SID JONES, DUM, PHD, DACUP PROSECTOR: DOUGLAS HERNDON DOSE GROUP: 1 DEATH: 96 STUDY DAY OF POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL DATE AND TIME OF NECROPSY: 07/15/86 8:32 SEX: MALE DATE OF DEATH: 07/15/86 ANIMAL NUMBER: B08372

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRTA, THORACIC (AD), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W.STEM (BR), CECUM (CE), COLON (CO), CORO, CERVICAL (CS), CORO, LUMBAR (LC), CORO, THORACIC (TC),
DUODENUM (DU), EPIDIOYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIUGR (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG),
MAND SALIUARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERUE, SCIATIC (SN), PANCREAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL UESICLE (SU), SKIN (SK), SKIN, OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR),
URINARY BLADDER (UB) THE FOLLOWING DRGANS WERE UNREMARKABLE AT NECROPSY:

FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SE),

BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),

DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILCUM (IL), JEJUNUM (JE), LACRIMAL GL, EXO (EO),

LIVER (LI), LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM),

NERUE, SCIATIC (SN), PANCREAS (PA), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SU), SKIN (SK),

SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR),

URINARY BLADDER (UB) 품

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/TOX SYSTEM CUTPUT ***

PRINTED: 12-MAY-88

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

H: 96 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 588.4 PROSECTOR: DOUGLAS HERNDON PATHOLOGIST: SID JONES, DUM, PHD, DACUP STUDY DAY OF DEATH: 96 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL DATE AND TIME OF NECROPSY: 07/15/86 10:08 DATE OF DEATH: 07/15/86 ANIMAL NUMBER: B08373

TERMINAL BODY WEIGHT: 588.4 GRAMS RECORDER: SID JONES, DUM, PHD, DACUP WEIGHER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

PATHOLOGY OBSERVATIONS CLINICAL OBSERVATIONS

-APPEARED NORMAL

COLLECTED/TAKEN (XW) :

NECROPSY

-ELECTRON MICROSCOPY SAMPLE; LIVER >NOTE:>EXTERNAL OBSERVATIONS:NONE GENERAL INFORMATION (XX):

INFILTRATION, LYMPHOID, -SLIGHT -PERIBRONCHIAL/PERIUASCULAR CUNG CLUS

-BILE DUCT, INFLAMMATION, CHRONIC,--FOCI OF MONONUCLEAR CELLS, -MINIMAL

AININI FEMINIE

HISTOPATHOLOGY

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AD), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR), THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY: URINARY BLADDER (UB)

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AD), BONE, FEMUR (FE), BONE, SIERMUM (SB),
BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORO, CERVICAL (CS), CORO, LUMBAR (LC), CORO, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HI), ILEUM (IL), JEJUNUM (JE), KIONEY (KD),
LACRIMAL GL, EXO (EO), LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE),
MUSCLE, SKELETAL (SM), NERUE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PI), PITUITARY (PI), PROSTATE (PR),
RECTUM (RE), SEMINAL UESICLE (SU), SKIN (SK), SPLEEN (SP), STOMACH, GL (SI), STOMACH, NONGL (SU), TESTIS (TE),
THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB) FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: 포

APPENDIX 8 *** PATH/TOX SYSTEM GUTPUT *** SUBCHRONIC TOXICITY STUDY IN RATS

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	ND I QUI	INDIVIDUAL ANIMAL SUMMARY REPORT		STUDY NUMBER: 2399108
ANIMAL NUMBER: B08374 SEX: MALE DATE OF DEATH: 07/15/86 STUDY DAY OF DATE AND TIME OF NECROPSY: 07/15/86 15:18 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL	DEATH	DOSE GROUP: 1 SACRIFICE STATUS: 96 STUDY WEEK OF DEATH: 14 PROSECTOR: BARBARA DAY PATHOLOGIST: SID JONES, DUM, PHD, DACUP	SCHE	DULED, TERMINAL SACRIFICE INAL BODY WEIGHT: \$24.3 GRAMS RECORDER: SID JONES, DUM, PHD, DACUP WEIGHER: BARBARA DAY
DRGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (*)	ORGAN TO BRAIN WEIGHT RATIO	ORGAN STATUS
		3 COOC	. 0240	WEIGHT TAKEN
BRAIN LIVETEM (BR)	2.00	3.000	1.000	WEIGHT TAKEN
	1.19	.227 %	.595	WEIGHT TAKEN
COL FER COD	1.04	198 %	.520	WEIGHT TAKEN
KIDNEY (KD)	3.26	622 %	1.630	•
LIUER (LI)	13.20	2.518 %	009.9	WEIGHT TAKEN
TESTIS/EPIDID (TP)	4.78	.912 %	2.390	WEIGHT TAKEN
CLINICAL OBSERVATIONS	HLAG	OLOGY OBSERUATIONS NECROPSY	SNO	HISTOPATHOLOGY
-APPEARED NORMAL	GENERAL INFI	NERAL INFORMATION (XX); >NOTE:>EXTERNAL OBSERUATIONS:NONE	HEART (HT): -CARDIOMYOPCARDIOMYOPCARDIOMYOPPERIBRONCH INFILTRATI PARATHYROJD >SECTION EX	HEART (HI): -CARDIOMYOPATHY, DEGENERATIVE,-MINIMAL LUNG (LU): -PERIBRONCHIAL/PERIVASCULAR, INFILTRATION, LYMPHOID,-SLIGHT PARATHYROID (PT): >SECTION EXAMINED; TISSUE NOT PRESENT

APPENDIX 8 *** PATH/IDX SYSTEM OUTPUT *** SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88 PACF: 188

STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

RECORDER: SID JONES, DUM, PHD, DACUP SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE WEIGHER: BARBARA DAY TERMINAL BODY WEIGHT: PATHOLOGIST: SID JONES, DUM, PHD, DACUP STUDY WEEK OF DEATH: 14 PROSECTOR: BARBARA DAY DOSE GROUP: 1 DEATH: 96 STUDY DAY OF POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL DATE AND TIME OF NECROPSY: 07/15/86 15:18 DATE OF DEATH: 07/15/86 NUMBER: 808374 ANIMA

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRIA, THORACIC (AD), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W.STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), DEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (ED), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR),
URINARY BLADDER (UB), ^COLLECTED/TAKEN (XW) THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),

BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),

DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), ILEUM (IL), JEJUNUM (JE), KIONEY (KD), LACRIMAL GL, EXO

, LIVER (LI), LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE),

MUSCLE, SKELETAL (SM), NERUE, SCIATIC (SN), PANCREAS (PA), PITUITARY (PI), PROSTATE (PR), RECTUM (RE),

SEMINAL VESICLE (SV), SKIN (SK), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH),

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/TOX SYSTEM OUTPUT ***

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INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE PATHOLOGIST: SID JONES, DUM, PHD, DACUP STUDY WEEK OF DEATH: 14 PROSECTOR: BARBARA DAY DOSE GROUP: 1 DEATH: 97 STUDY DAY OF POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL 8:38 SEX: MALE DATE AND TIME OF NECROPSY: 07/16/86 DATE OF DEATH: 07/16/86 ANIMAL NUMBER: B08375

TINAL BODY WEIGHT: 459.3 GRAMS RECORDER: SID JONES, DUM, PHD, DACUP WEIGHER: NOT REQUIRED BY PROTOCOL TERMINAL BODY WEIGHT:

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

CLINICAL OBSERUATIONS

-APPEARED NORMAL

LUNG (LU) : OBSERUATIONS ^COLLECTED/TAKEN (XW) :
-ELECTRON MICROSCOPY SAMPLE; LIVER GENERAL INFORMATION (XX) : NECROPSY PATHOLOGY

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SECTION EXAMINED; TISSUE NOT PRESENT INFILTRATION, LYMPHOID, -SLIGHT -PERIBRONCHIAL/PERIUASCULAR MAMMARY GLAND (MG): NOTE: VEXTERNAL OBSERVATIONS: NONE

HISTOPATHOLOGY

DUGDENUM (COLTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AD), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W.STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
BUDDENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (ES),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR), THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY: URINARY BLADDER (UB)

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRIA, THORACIC (AD), BONE, FEMIR (FE), BONE, SIERNUM (SB),
BRAIN WASTEM (BR), CECUM (CE), COLON (CD), CORO, CERVICAL (CS), CORO, LUMBAR (LC), CORO, THORACIC (TC),
BUDDOBNUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIONEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), MAND SALIVARY GL (SG), MARROW, STERNUM (SE),
MUSCLE, SKELETAL (SM), NERUE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR),
RECTUM (RE), SEMINAL UESICLE (SU), SKIN (SK), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE),
THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (IB) FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: 프

APPENDIX B *** PATH/TOX SYSTEM OUTPUT *** SUBCHRONIC TOXICITY STUDY IN RATS

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STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: B08376 SEX: MALE DATE OF DEATH: 07/16/86 STUDY DAY OF DATE AND TIME OF NECROPSY: 07/16/86 8:47 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL	DEATH	DOSE GROUP: 1 SACRIFICE STATUS: 1: 97 STUDY WEEK OF DEATH: 14 PROSECTOR: TIM GROVE PATHOLOGIST: SID JONES, DVM, PHD, DACUP	SCHE	SCHEDULED, TERMINAL SACRIFICE TERMINAL BOOY WEIGHT: 518.8 GRAMS . RECORDER: SID JONES, DUM, PHD, DACUP WEIGHER: TIM GROUE
DRGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO	ORGAN STATUS
ADRENAL (AD) BRAIN W.STEM (BR) HEART (HT) SPLEEN (SP) KIDNEY (KD) LIVER (LI) TESTIS/EPIDID (TP)		.0108 % .387 % .262 % .172 % .619 % 2.862 %	1.600 1.000 .627 .443 1.597 7.388	MEIGHT TAKEN
CLINICAL OBSERVATIONS	⊢ ♥ d	HOLOGY OBSERVATIONS NECROPSY	SZO	HISTOPATHOLOGY
-APPEARED NORMAL	GENERAL INFO	GENERAL INFORMATION (XX):	LUNG (LU): - PERIBROHCH INFILTRATI	NG (LU): -PERIBROMCHIAL/PERIVASCULAR, INFILTRATION, LYMPHOID,-SLIGHT

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/TOX SYSTEM DUTPUT *** APPENDIX 8

PRINTED: 12-MAY-88

STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

TERMINAL BODY WEIGHT: 518.8 GRAMS RECORDER: SID JONES, DUM, PHD, DACUP SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE WEIGHER: TIM GROUE PATHOLOGIST: SID JONES, DUM, PHD, DACUP STIJDY WEEK OF DEATH: 14 PROSECTOR: TIM GROVE DOSE GROUP: 1 DEATH: 97 OF DEATH: 07/16/86 STUDY DAY OF AND TIME OF NECROPSY: 07/16/86 8:47 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL SEX: MALE ANIMAL NUMBER: 808376 DATE OF DEATH: 07/16/86 DATE

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRIA, THORACIC (AD), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN WYSTEM (BR), CECUM (CC), CORO, CORO, CORO, LUMBAR (LC), CORO, THORACIC (TC),
BRAIN WYSTEM (BR), CECUM (CC), COLON (CO), CORO, CORO, LUMBAR (LC), DEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS),
SPLEEN (SP), STOMACH, GL (SI), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR), THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRTA, THORACIC (AD), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIOYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), MAMMARY GLAND (MS), MAND SALIVARY GL (SG),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI),
PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SPLEEN (SP), SIOMACH, GL (ST), STOMACH, NOMGL (SU), FESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB) FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: 뿔

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/TOX SYSTEM OUTPUT *** APPENDIX 8

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INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

492.3 GRAMS SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE TERMINAL BODY WEIGHT: PATHOLOGIST: SID JONES, DUM, PHD, DACUP STUDY WEEK OF DEATH: 14 PROSECTOR: BARBARA DAY DOSE GROUP: 1 STUDY DAY OF DEATH: 97 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL 9:59 DATE AND TIME OF NECROPSY: 07/16/86 DATE OF DEATH: 07/16/86 ANIMAL NUMBER: B08377

RECORDER: SID JONES, DUM, PHD, DACUP WEIGHER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO DRGAN WEIGHTS RECORDED ***

CLINICAL OBSERVATIONS

-APPEARED NORMAL

INFILTRATION, LYMPHOID, -MODERATE -PERTERONCHIAL /PERTUASCULAR HISTOPATHOLOGY CONG (CID) 08SERUATIONS -ELECTRON MICROSCOPY SAMPLE; LIVER >NOTE:>EXTERNAL OBSERVATIONS:NONE GENERAL INFORMATION (XX) : NECROPSY COLLECTED/TAKEN (XW) PATHOLOGY

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRIA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
BRAIN W/STEM (BR), CECUM (CE), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJINNUM (JE), KIONEY (KD),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (LM), LUNG (LU), MAMMARY GLAND (MG),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERUE, SCIATIC (SM), PANCREAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB)

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRIA, THORACIC (AO), BONE, FEMINR (FE), BONE, STERNUM (SB),
BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUDDENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIUER (LI), LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIUARY GL (SG),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERUE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PI), PITUITARY (PI),
PROSTATE (PR), RECTUM (RE), SEMINAL UESICLE (SU), SKIN (SK), SPLEEN (SP), STOMACH, GL (SI), STOMACH, NONGL (SU),
TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLANDER (HB) FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: 뽀

APPENDIX 8 *** PATH/TOX SYSTEM OUTPUT *** SUBCHRONIC TOXICITY STIDY IN RATS

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	OLUIONI	NDIUIDUAL ANIMAL SUMMARY REPORT		STUDY NUMBER: 2399108
ANIMAL NUMBER: 808378 SEX: MALE DATE OF DEATH: 07/16/86 STUDY DAY OF DATE AND TIME OF NECROPSY: 07/16/86 10:57 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL	F DEATH L	DOSE GROUP: 1 SACRIFICE STATUS: 1: 97 STUDY WEEK OF DEATH: 14 PROSECTOR: TIM GROVE PATHOLOGIST: SID JONES, DUM, PHD, DACUP	SCHE	DULED, TERMINAL SACRIFICE INAL BODY WEIGHT: 498.1 GRAMS RECORDER: SID JOHES, DUM, PHD, DACUP WEIGHER: TIM GROUE
ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO	ORGAN
! ~	.057	.0114 %	.0270	i
BRAIN W/STEM (BR)	2.11 1 44	. 424 % 0.00 %	1.000	WEIGHT TAKEN MFIGHT TAKEN
	72.	. 153 %	.360	
	3,35	.673 %	1.588	WEIGHT TAKEN
_	17.18	3.449 %	8.142.	WEIGHT TAKEN
TESTIS/EPIDID (TP)	5.00	1.004 %	2.370	WEIGHT TAKEN
CLINICAL OBSERVATIONS	PATHOL	HOLOGY OBSERUATI NECROPSY	o z	нгэторатногосу
-APPEARED NORMAL	GENERAL 14FC	NERAL INFORMATION (XX); >NOTE:>EXTERNAL DBSERVATIONS:NONE	ADRENAL, CORTEX (AC): -UACUOI IZATION,-SLIGHT LACRIMAL GL, EXD (EO): -FOCAL MONONICLEAR INF LUNG (LU): -PERIBRONCHIAL/PERIUAS INFILTRATION, LYMPHOI TESTIS (TE): -DEGENERATION, SLIGHT	RENAL, CORTEX (AC): -UACUOLIZATION,-SLIGHT -CRIMAL GL, EXD (ED): -FOCAL MONONICLEAR INFILTRATE,-MINIMAL ING (LU): -PERIBRONCHIAL/PERIUASCULAR, INFILTRATION, LYMPHOID,-SLIGHT -DEGENERATION,-SLIGHT
	:			

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/TOX SYSTEM DUTPUT *** APPENDIX B

PRINTED: 12-MAY-88

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

TERMINAL BODY WEIGHT: 498,1 GRAMS RECORDER: SID JONES, DUM, PHD, DACUP SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE WEIGHER: TIM GROUE PATHOLOGIST: SID JONES, DUM, PHD, DACUP STUDY WEEK OF DEATH: 14 PROSECTOR: TIM GROUE DOSE GROUP: 1 DATE OF DEATH: 07/16/86 STUDY DAY OF DEATH: 97
DATE AND TIME OF NECROPSY: 07/16/86 10:57 PROSE POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL SEX: MALE ANIMAL NUMBER: 808378

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRTA, THORACIC (AO), BONE, FEMUR (FE), BOHE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUDDDENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR),
URINARY BLADDER (UB), ^COLLECTED/TAKEN (XW)

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FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNUM (SB), BRAIN WASTEM (BR), CECUM (CE),
COLON (CO), CORD, CERUICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC), DUODENUM (DU), FPIDIDYMIS (FP),
ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LIVER (LI), LN, MESENTERIC (MS),
MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), MERUE, SCIATIC (SN),
PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SU), SKIN (SK),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB)

APPENDIX 8 *** PATH/IOX SYSTEM OUTPUT *** SUBCHRONIC TOXICITY STUDY IN RATS

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STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: B08379 SEX: MALE DOS DATE OF DEATH: 07/16/86 STUDY DAY DF DEATH: 97 DATE AND TIME OF NECROPSY: 07/16/86 14:13 PROSE POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL PATHO	SEX: MALE DOSE GROUP: 1 STUDY DAY DF DEATH: 97 STUDY 16/86 14:13 PROSECTOR: TIM BY PROTOCOL PATHOLOGIST: SI	WEEK C GROUE D JONES	SCHE	DULED, TERMINAL SACRIFICE INAL BODY WEIGHT: 494.7 GRAMS RECORDER: SIO JONES, DUM, PHD, DACUP WEIGHER: TIM GROUE
ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO	ORGANSTATUS
ADRENAL (AD) BRAIN W/STEM (BR)	2.01	. 0101 %	1.000	<u></u>
	1.23	. 249 % . 109 %	.612	F- ,-
KIDNEY (KD)	2.85	.576 % 2.587 %	1.418	LEIGHT TAKEN WEIGHT TAKEN
TESTIS/EPIDID (TP)		× 906.	2.229	WEIGHT TAKEN
CLINICAL OBSERVATIONS	C C.	THOLOGY OBSERUATIONS NECROPSY	8 N O	HISTOPATHOLDGY
-APPEARED NORMAL	GENERAL INFO	GENERAL INFORMATION (XX): >NOTE:>EXTERNAL OBSERVATIONS:NONE	KIDNEY (KD): -NEPHROPATHY MINIMAL LIUGR (LI): -BILE DUCT;	DNEY (KD): -NEPHROPATHY, CHRONIC PROGRESSIVE,- MINIMAL VER (LI): -BILE DUCT, INFLAMMATION, CHRONIC,- MINIMAL

LUNG (LI):
-PERIBRONCHIAL/PERIUASCULAR,
INFILTRATION, LYMPHCID,-SLIGHT

APPENDIX 8 *** PATH/IOX SYSTEM OUTPUT *** SUBCHRONIC TOXICITY STUDY IN RATS

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STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

TERMINAL BODY WEIGHT: 494.7 GRAMS RECORDER: SID JONES, DUM, PHD, DACUP SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE WEIGHER: TIM GROUE PATHOLOGIST: SID JONES, DUM, PHD, DACUP STUDY WEEK OF DEATH: 14 PROSECTOR: TIM GROUE DOSE GROUP: 1 DATE OF DEATH: 07/16/86 STUDY DAY OF DEATH: 97
DATE AND TIME OF NECROPSY: 07/16/86 14:13 PROSE POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL SEX: MALE ANIMAL NUMBER: B08379

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRTA, THORACIC (AD), BOWE, FEMUR (FE), BOWE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), CORO, CORO, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUDDENUM (DU), EPIDIOYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANGREAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SU), SKIN (SK), SKIN, OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR),
URINARY BLADDER (UB), COLLECTED/TAKEN (XW) THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRTA, THORACIC (AD), BONE, FEMUR (FE), BONE, STERNUM (SB),

BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),

DUDDENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), LACRIMAL GL, EXD (ED),

LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM),

NERUE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV)

, SKIN (SK), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY),

TRACHEA (TR), URINARY BLADDER (UB)

APPENDIX 8 *** PATH/TOX SYSTEM DUTPUT *** SUBCHRONIC TOXICITY STUDY IN RAIS

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	GINIGNI	INDIVIDUAL ANIMAL SUMMARY REPORT	1	STUDY NUMBER: 2399108
ANIMAL NUMBER: B08380 SEX: MALE DATE OF DEATH: 07/16/86 STUDY DAY OF DATE AND TIME OF NECROPSY: 07/16/86 14:44 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL	DEATH	WEEK O GROUE D JONES	SCHE	SCHEDULED, TERMINAL SACRIFICE TERMINAL BODY WEIGHT: 554.1 GRAMS RECORDER: SID JONES, DUM, PHD, DACUP WEIGHER: TIM GROVE
DRGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN WEJGHT RATIO	ORBAN STATUS
ADREMAL (AD) BRAIN WYSTEM (BR)	.057	0103 %	.0288	
IT)	1.45	.262 % .168 %	.732	, ,
KIDNEY (KD) LIVER (LI) TESTIS/EPIDID (TP)	3.65 13.30 5.06	.659 % 2.400 % .913 %	1.843 6.717 2.556	WEIGHT TAKEN WEIGHT TAKEN WEIGHT TAKEN
CLINICAL DBSERVATIONS	F A G	HOLOGY OBSERUATIONS	SZO	ніѕторатногосх
-APPEARED NORMAL	GENERAL INFO	GENERAL INFORMATION (XX): >NOTE:>EXTERNAL OBSERVATIONS:NONE	LUNG (LU): -PERIBRONCHIAL/PE INFILTRATION, LY PARATHYROID (PT): >SECTION EXAMINED	NG (LU): -PERIBRONCHIAL/PERIUASCULAR, INFILTRATION, LYMPHOID,-SLIGHT RATHYROID (PT): >SECTION EXAMINED; TISSUE NOT PRESENT

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/TOX SYSTEM DUTPUT *** APPENDIX 8

PRINTED: 12-MAY-88

STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

RECORDER: SID JONES, DUM, PHD, DACUP 554.1 GRAMS SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE TERMINAL BODY WEIGHT: WEIGHER: TIM GROVE PATHOLOGIST: SID JONES, DUM, PHD, DACUP STIJDY WEEK OF DEATH: 14 PROSECTOR: TIM GROVE DOSE GROUP: 1 OF DEATH: 97/16/86 STUDY DAY OF DEATH: 97 AND TIME OF NECROPSY: 07/16/86 14:44 PRISE POST-FIX WEIGHER: NOT REGUIRED BY PROTOCOL SEX: MALE DATE OF DEATH: 87/16/86 NUMBER: B08380 DATE

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AGRIA, THORACIC (AD), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUGDENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXD (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MS),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), MERUE, SCIATIC (SN), PANCREAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SU), SKIN (SK), SKIN, OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR),
URINARY BLADDER (UB), ACOLLECTED/TAKEN (XW)

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AG), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUDDENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIONEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANGREAS (PA), PITUITARY (PI), PROSTATE (PR),
RECTUM (RE), SEMINAL VESICLE (SU), SKIN (SK), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NORGL (SU), TESTIS (TE),
THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB) THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

APPENDIX 8 *** PATH/TOX SYSTEM OUTPUT *** SUBCHRONIC TOXICITY STUDY IN RATS

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STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: B08381 SEX: MALE DATE OF DEATH: 07/16/86 STUDY DAY OF DATE AND TIME OF NECROPSY: 07/16/86 14:52 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL	DEATH	MEEK O	SCHE	SCHEDULED, TERMINAL SACRIFICE TERMINAL BODY WEIGHT: 479.0 GRAMS RECORDER: SID JONES, DVM, PHD, DACUP WEIGHER: BARBARA DAY
ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	DRGAN TO BRAIN WEIGHT RATIO	0 R G A N S T A T U S
ADRENAL (AD) BRAIN W/STEM (BR)	.059	. 453 %	. 0272	
HEART (HT) SPLEEN (SP)	1.25	. 192 %	.424	WEIGHT TAKEN
KIDNEY (KD) LIUER (LI) TESTIS/EPIDID (TP)	. 2,70 9,99 5,25	.564 % 2.086 % 1.096 %	1.244 4.604 2.419	WEIGHT TAKEN
CLINICAL OBSERVATIONS	PATHOLOGY	DBSERUATI	SZO	HISTOPATHOLOGY
-APPEARED NORMAL	GENERAL INFO	ERAL INFORMATION (XX):	LOGENIAL GL, EXO -FOCAL MONONUCLI LUNG (LU): -PERJBRONCHIAL/I INFILTRATION, I THYMUS (TH): >TISSUE MISSING	LACRIMAL GL, EXO (ED): -FOCAL MONONUCLEAR INFILTRATE,-MINIMAL LUNG (LU): -PERIBRONCHIAL/PERIVASCULAR, INFILTRATION, LYMPHOID,-SLIGHT THYMUS (TH): >TISSUE MISSING

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/TOX SYSTEM OUTPUT *** APPENDIX 8

PRINTED: 12-MAY-88

STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

RECORDER: SID JONES, DUM, PHD, DACUP 479.0 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE WEIGHER: BARBARA DAY TERMINAL BODY WEIGHT: PATHOLOGIST: SID JONES, DUM, PHD, DACUP STUDY WEEK OF DEATH: 14 PROSECTOR: BARBARA DAY DOSE GROUP: 1 DATE OF DEATH: 07/16/86 STUDY DAY OF DEATH: 97
DATE AND TIME OF NECROPSY: 07/16/86 14:52 PROSE POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL SEX: MALE ANIMAL NUMBER: B08381

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMIN (FE), BONE, STERNUM (SB),
BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORD, CERUICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNIM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANGREAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR),
URINARY BLADDER (UB), ~COLLECTED/TAKEN (XW)

FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: 분

ADRENAL, CORTEX (AC), AORENAL, MEDULLA (AM), AORTA, THORACIC (AD), BONE, FEMIJR (FE), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LIVER (LI), LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROLL, STERNUM (SE), MUSCLE, SKELETAL (SM),
NERUE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE),
SEMINAL VESICLE (SU), SKIN (SK), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYROID (TY),
TRACHEA (TR), URINARY BLADDER (UB)

A** PATH/IDX SYSTEM OUTPUT *** SUBCHRONIC TOXICITY STUDY IN RATS

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INDIVIDUAL ANIMAL SUMMARY REPURT

STUDY NUMBER: 2399108

TERMINAL BODY WEIGHT: 265.5 GRAMS RECORDER: JAMES CANNON SACRIFICE STATUS: UNSCHEDULED (M) 4: 13 STUDY WEEK OF DEATH: 2 PROSECTOR: JAMES CANNON PATHOLOGIST: NOT REQUIRED BY PROTOCOL DOSE GROUP: 2 DATE OF DEATH: 04/23/86 STUDY DAY OF DEATH: 13
DATE AND TIME OF NECROPSY: 04/23/86 15:07 PROSEI
POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL PATHOL ANIMAL NUMBER: B08402

WEIGHER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

CLINICAL OBSERVATIONS

-APPEARED NORMAL

√S HISTOPATHOLOGY	BONE, FEMUR -ARTICULAR LIVER (LI) : -FOCI OF MO LN, OTHER (L -HYPERFLASI MAMMARY GLAND > SECTION EX SKIN, OTHER -INFLAMMATI
PATHOLOGY OBSE NECROPSY	LIUGER (LI): 'H-ENLARGED LN, OTHER (LN): -ENLARGED; MANDIBULAR SKIN, OTHER (SS): -SORE; RIGHT LATERAL NECK, CHE, CRUSTY, OPEN, MARGINS NECROTIC, TAN TO DARK RED, 2.0 x 2.0 CM; LEFT LATERAL NECK, DNE, CRUSTY, OPEN, TAN TO DARK RED, 1.0 x 1.0 CM GENERAL INFORMATION (XX): NOTE:>REASON FOR SACRIFICE AND NOTE:>REASON FOR SACRIFICE AND NECROTIC SORES, SECTIONS:NECK-

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/TOX SYSTEM DUTPUT *** APPENDIX 8

INDIVIDUAL ANIMAL SUMMARY REPORT

PRINTED: 12-MAY-88

STUDY NUMBER: 2399108

RECORDER: JAMES CANNON TERMINAL BODY WEIGHT: SACRIFICE STATUS: UNSCHEDULED (M) PATHOLOGIST: NOT REDUIRED BY PRITICOL STUDY WEEK OF DEATH: 2 PROSECTOR: JAMES CANNON DOSE GROUP: 2 STUDY DAY OF DEATH: 13 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL AND TIME OF NECROPSY: 04/23/86 15:07 SEX: MALE DATE OF DEATH: 04/23/86 ANIMAL NUMBER: B08402 DATE

WEIGHER: NOT REQUIRED BY PROTOCOL

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRIA, THORACIC (AD), BONE, FEMIR (FE), BONE, STERNUM (SB),
BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUDDENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HI), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXD (EO), LN, MESENTERIC (MS), LUNG (LU), MAMMARY GLAND (MG), MAND SALIUARY GL (SG), MARROW, STERNUM (SE),
MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PI), PITUITARY (PI), PROSTATE (PR),
RECTUM (RE), SEMINAL UESICLE (SU), SKIN (SK), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONSL (SU), TESTIS (TE),
THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (IB), ^COLLECTED/TAKEN (XW) THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AD), BONE, STERNIM (SB), BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORO, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC), DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXO (EO), LACRIMAL (EN), LUNG (LU), MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SU), SKIN (SK), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB) FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: 뿔

SUBCHRONIC TOXICITY STUDY IN PATS *** PATH/IOX SYSTEM OUTPUT *** APPENDIX 8

PRINTED: 12-MAY-88

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

PATHOLOGIST: SID JONES, DUM, PHD, DACUP STUDY WEEK OF DEATH: 14 PROSECTOR: TIM GROUE DOSE GROUP: 2 STUDY DAY OF DEATH: POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL DATE OF DEATH: 02/14/86 STUDY DAY OF DATE AND TIME OF NECROPSY: 02/14/86 9:18 SEX: MALE ANIMAL NUMBER: 808403

TERMINAL MODY WEIGHT: 516.3 GRAMS
RECORDER: SID JONES, DUM, PHD, DACUP
WEIGHER: NOT REGUIRED BY PROTOCOL SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

OBSERUATIONS NECROPSY PATHOLOGY

CLINICAL OBSERVATIONS

-APPEARED NORMAL

RIGHT, FLUID FILLED : (MX) RIGHT, YELLOW ~COLLECTED/TAKEN RIGHT -SOFT; -PALE; -CYST;

-DEGENERATION,-MODERATELY SEVERE INFILTRATION, LYMPHOID, MINIMAL

TESTIS (TE):

-PERTERONCHIAL/PERTUASCULAR

LUNG (LU)

HISTOPATHOLOGY

-ELECTRON MICROSCOPY SAMPLE; LIVER >NOTE:>EXTERNAL DBSERVATIONS:NONF GENERAL INFORMATION (XX) :

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRIA, THORACIC (AD), BDNE, FEMUR (FE), BDNE, STERNUM (SB),
BRAIN WASTEM (BR), CECUM (CE), COLON (CD), CORD, CERVICAL (CS), CORD, LIMBAR (LC), CORD, THORACIC (TC),
BUDDENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTFRIC (MS), LN, OTHER (LN), LUNG (LI), MAMMARY SLAND (MS),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SU), SKIN (SK), SKIN, OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB) THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: KIDNEY (KD), LIVER (LI) 뿔

APPENDIX B *** PATH/TOX SYSTEM OUITPUT *** SUBCHRONIC TOXICITY STUDY IN RAIS

PRINTED: 12-MAY-88 PAGE: 214

STUDY MUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT .

ANIMAL NUMBER: B08404 SEX: MALE DATE OF DEATH: 07/14/86 STUDY DAY OF DATE AND TIME OF NECROPSY: 07/14/86 8:45 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL	DEATH	DOSE GROUP: 2 SACRIFICE STATUS: 1: 95 STUDY WEEK OF DEATH: 14 PROSECTOR: TIM GROUE PATHOLOGIST: SID JONES, DUM, PHD, DACUP	SCHE	SCHEDULED, TERMINAL SACRIFICE TERMINAL BODY WEIGHT: \$12.3 GRAMS RECORDER: SID JONES, DUM, PHD, DACUP WEIGHER: TIM GROUE
	ABSOLU	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO	ORGAN STATUS
ADRENAL (AD)	. 044	% 9800°	. 0208	MEIGHT TAKEN
BRAIN W/STEM (BR)	2.12	.414 X	1.000	WEIGHT TAKEN
HEART (HT)	1.40	.273 %	.660	METCHT TAKEN
SPLEEN (SP)	.74	.144 %	.349	WEIGHT TAKEN
KIDNEY (KD)	3.31	. 646 %	1.561	MEIGHT TAKEN
LIVER (LI)	14.75	2.879 %	6.958	MEIGHT TAKEN
TESTIS/EPIDID (TP)	5.46	1.066 %	2,575	MEIGHT TAKEN
CLINICAL OBSERVATIONS	C C	THOLOGY OBSERUATIONS NECROPSY	S Z O	HISTOPATHOLOGY
-APPEARED NORMAL	GENERAL INF	GENERAL INFORMATION (XX): >NOTE:>EXTERNAL OBSERVATIONS:MONE	LUNG (LLI) : -PERIBRUMD: INFILTRATI	NG (LU): -PERIBRUMCHIAL/PERIVASCULAR, INFILTRATION, LYMPHOID,-MINIMAL

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (CA), THORACIC (AC), BORIE, FEMIR (FE), BORIE, STERNUM (SB),
BRAIN WESTEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJURUM (JE), KIONEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MS),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR),
URINARY BLADDER (UB), COLLECTED/TAKEN (XW) THE FOLLOWING DRGANS WERE UNREMARKABLE AT NECROPSY:

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: KIDNEY (KD), LIVER (LI)

^{***.} ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) MERE SAVED ***

APPENDIX 8 *** PATH/TOX SYSTEM OUTPUT *** SUBCHRONIC TOXICITY STUDY IN RATS

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STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

TERMINAL BODY WEIGHT: 492.8 GRAMS RECORDER: SID JONES, DUM, PHD, DACUP -FOCI OF MONONICLEAR CELLS, -MINIMAL TAKEN WEIGHT TAKEN TAKEN TEKEN NE XEL TAKEN TAKEN STATUS 0 R G A N HISTOPATHOLOGY SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE WE I GHT WE I GHT LE I SHT WE IGHT WE JOHT WE I SHI WEIGHER: TIM GROVE ([] ORGAN TO BRAIN WEIGHT RATIO . 0229 6.432 629. . 442 1.0002.416 1.611 PATHOLOGIST: SID JONES, DUM, PHD, DACUP STUDY WEEK OF DEATH: 14 ORGAN WEIGHT RELATIVE >NOTE:>EXTERNAL OBSERVATIONS:NOHE TO BODY WEIGHT (%) OBSERU .0093 .407 .277 .180 .656 2.619GENERAL INFORMATION (XX) NECROPSY PROSECTOR: TIM GROUE DOSE GROUP: 2 ATHOLOGY ABSOLUTE ORGAN WEIGHT DEATH: 96 (GRAMS) ----. 046 1.36 .89 3.23 12.91 4.85 2.01 DATE OF DEATH: 07/15/86 STUDY DAY OF DATE AND TIME OF NECROPSY: 07/15/86 8:09 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL SEX: MALE CLINICAL OBSERVATIONS (FE) FEST1S/EP1010 NUMBER: 808405 BRAIN W/STEM (GP) (SP) 8 Œ (1) DREAN NAME -APPEARED NORMAL ADRENAL SPLEEN KIDMEY **FEART** LIVER ANIMAL

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRIA, THORACIC (AD), BOHE, FEMUR (FE), BOHE, STERNUM (SB),
BRAIN W.STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUDDENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), ABJURUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (L1), MAMMARY GLAND (MS),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERUE, SCIATIC (SN), PARCHEAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SU), SKIN (SK), SKIN, OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMIS (TH), THYROID (TY), TRACHEA (TR),
URINARY BLADDER (UB), ACOLLECTED/TAKEN (XW) THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

INFILTRATION, LYMPHOID, - SLIGHT

-PERTERONCHIAL/PERTUASCULAR

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: KIDNEY (KD)

^{***} ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

*** PATH/TOX SYSTEM OUTPUT *** SUBCHRONIC TOXICITY STUDY IN RAIS

PRINTED: 12-MAY-80 PAGE: 206

STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPURT

ANIMAL NUMBER: B08406 SEX: MALE DATE OF DEATH: 07/15/86 STUDY DAY OF DATE AND TIME OF NECROPSY: 07/15/86 10:27 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL	DEATH	WEEK D SROVE JONES	SCHE	SCHEDULFD, TERMINAL SACRIFICE TERMINAL BOOY WEIGHT: 515.8 GRAMS RECORDER: SID JONES, DUM, PHD, DACUP WEIGHER: TIM GROUE
ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORIGAN TO BRAIN METGHT RATTO	0 R G A N S T A T U S
ADRENAL (AD) BRAIN W/STEM (BR)	. 054	.0105 %	. 8260 1.008	WEIGHT TAKEN WEIGHT TAKEN
	1.22	237 %	.591	
KIDNEY (KD)	3.08	% 866°	1.487	
5	12.85	2,490 % 933 %	6.194 2.319	WEIGHT TAKEN WEIGHT TAKEN
CLINICAL DBSERVATIONS	G.	ATHOLOGY OBSERUATIONS NECROPSY	5 4 7 7 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	HISTOPATHOLOGY
- APPEARED NORMAL	GENERAL INFO	NERAL INFORMATION (XX):	KIDNEY (KD):	DNEY (KD):

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRIA, THORACIC (AD), BINE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W.STEM (BR), CECUM (CC), CORO, CERUICAL (CS), CIRD, LUMBAR (LC), CORD, THORACIC (TC),
BUGDENUM (DU), EPIDIOYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EQ), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUMS (LI), MAMMÉRY GLAMO (MS),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MISCLE, SKELETAL (SM), NERUE, SCIATIC (SN), PAUCREAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (FR), RECTUM (RE), SEMINAL VESICLE (SU), SKIN (SK), SKIN, OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR),
URINARY BLADDER (18), ACOLLECTED/TAKEN (XW)

THE FOLLOWING ORGANS WERE UNREMARKABLE AT MECROPSY:

INFILTRATION, LYMPHOID, - SLIGHT

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: LIVER (L1)

^{***} ALL ORGANSZIJSSUES (REQUIRED TO BE HARVESTED PER THE STIMY PROTOCH) MERE SAUED ***

APPENDIX 8 *** PATH/IOX SYSTEM DUTPUT *** SUBCHRONIC TOXICITY STILDY IN RATS

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STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: B08407 SEX: MALE DATE OF DEATH: 07/15/86 STUDY DAY OF DATE AND TIME OF NECROPSY: 07/15/86 13:53 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL	В	ROUP: 2 STUDY WEEK OR: BARBARA DAY	SCHE TERM	SCHEDULED, TERMINAL SACRIFICE TERMINAL BODY WEIGHT: 481.6 GRAMS RECORDER: SÍO JONES, OUM, PHD, DACUP WEIGHER: BARBARA DAY
ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	IT ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO	O R G A N S T A T U S
ADRENAL (AD)		. 9108 %	. 0241	METGHT TAKEN
BRAIN W/STEM (BR)	2.16	. 449 %	1.000	WEIGHT TAKEN
HEART (HT)	1.30	.271 %	.683	
SPLEEN (SP)	72.	.160 %	.357	
K1DNEY (KD)	2,78	. 578 %	1.288	WEIGHT TAKEN
LIVER (LI)	11.80	2.449 %	5.461	METGHT TAKEN
TESTIS/EPIDID (TP)	4.74	.984 %	2.194	WEIGHT TAKEN
	₹ 6	THOLOGY	SNO	
CLINICAL DESERVATIONS		NEURUPIN		H.S. (DPH MOLCOST
-APPEARED NORMAL	GENERAL)	GENERAL INFORMATION (XX) : >NOTE:>EXTERNAL ORSERVATIONS:NONE	LUNG (LU): -PERTERNICH INFILTRATI	NG (LU): -PERTERONCHIAL/PERTUASCULAR, INFILTRATION, LYMPHOID,-SLIGHT

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRTA, THDRACIC (AD), BONE, FEMINE (FE), BONE, STERNIM (SB),
BRAIN WASTEM (BR), CECUM (CE), COLON (CD), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THERACIC (TC),
BUDDENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUMG (LU), MAMMARY GLAND (MG),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERUE, SCIATIC (SN), PANCREAS (PA),
PARATHYROID (PT), PITULITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR),
URINARY BLADDER (UB), ~COLLECTED/TAKEN (XW) THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

-PNEUMONITIS, -MINIMAL

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: KIDNEY (KD), LIVER (LI)

^{***} ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/TOX SYSTEM QUITPUT *** APPENDIX 8

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INDIVIDUAL ANIMAL SUMMARY REPURT

STUDY NUMBER: 2399188

TERMINAL BODY WEIGHT: 473.1 GRAMS
RECORDER: SID JONES, DUM, PHD, DACUP
WEIGHER: NOT REQUIRED BY PROTOCOL SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE PATHOLOGIST: SID JONES, DUM, PHO, DAI'UP STUDY WEEK OF DEATH: 14 PROSECTOR: TIM GROUE DOSE GROUP: 2 STUDY DAY OF DEATH: 95 POST-FIX WEIGHER: NOT REGUIRED BY PROTOCOL DATE AND TIME OF NECROPSY: 07/14/86 10:53 SEX: MALE DATE OF DEATH: 07/14/86 ANIMAL NUMBER: B08408

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

HISTOPATHOLOGY LUNG (Lt) : OBSERUATIORS -ELECTRON MICROSCOPY SAMPLE; LIVER GENERAL INFIDRMATION (XX) : NECROPSY COLLECTED/TAKEN (XW) : PATHOLOGY CLINICAL OBSERVATIONS -APPEARED NORMAL

>HOTE:>EXTERNAL OBSERVATIONS:NOBLE

INFILTRATION, LYMPHOID, -SLIGHT -PERTRRONCHIAL /PERTUASCUL AR

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRIA, THORACIC (AD), BONE, FEMUR (FE), BINE, STERNUM (SB),
BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORO, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUDDENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREGS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR), ı ı THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY: URINARY BLADDER (UB)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: KIDNEY (KD), LIVER (LI)

APPENDIX 8 *** PATH/TOX SYSTEM OUTPUT *** SUBCHRONIC TOXICITY STEMY IN RAIS

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INDIVIDIAL ANTMAL SUMMARY REPORT

STLIDY NUMBER: 2399188

PATHOLOGIST: SID JONES, DUM, PHD, DACUP STUDY WEEK OF DEATH: 14 PROSECTOR: BARBARA DAY DOSE GROUP: 2 DEATH: 95 STUDY DAY OF POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL DATE AND TIME OF NECROPSY: 07/14/86 11:43 DATE OF DEATH: 07/14/86 ANIMAL NUMBER: 808409

SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
JF DEATH: 14 TERMINAL BROY WEIGHT: 471.7 GRAMS
RECORDER: SID JONES, DUM, PHD, DACUP
LEIGHFR: NOT REQUIRED BY PROTRICE.

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

CLINICAL OBSERVATIONS

-APPEARED NORMAL

PATHOLOGY OBSERVATIONS NECROPSY

^COLLECTED/TAKEN (XW):
-ELECTRON MICROSCOPY SAMPLE; LIVER
GENERAL INFORMATION (XX):
>NOTE:>EXTERNAL OBSERVATIONS:NONE

MINIMAL LUMG (LI): -PERIBRONCHIAL/PERIUASCULAR, INFILTRATION, LYMPHOID,-SLIGHT

-NEPHROPATHY, CHRONIC PROGRESSIVE,-

KIDNEY (KD)

HISTOPATHOLOGY

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRIA, THORACIC (AD), BONE, FEMUR (FE), BONE, STERNEM (SB),
BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
BRODENUM (DU), EPIDIDYMIS (EP), ESOPHAGIS (ES), EYE (EY), HEART (HI), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MS),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERUE, SCIATIC (SN), PANCREAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SU), SKIN (SK), SKIN, OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR), THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY: URINARY BLADDER (UB)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

APPENDIX 8 *** PATH/IDX SYSTEM OUTPUT *** SUBCHRONIC TOXICITY STUDY IN RAIS

PRINTED: 12-MAY-88 PAGE: 210

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

TERMINAL BODY WEIGHT: 492.8 GRAMS
RECGROER: SID JONES, DUM, PHD, DACUP
WEIGHER: NOT REQUIRED BY PROTOCOL. SACRIFICE STATUS: SCHEDULED, LERMINAL SACRIFICE PATHOLOGIST: SID JONES, DUM, PHO, DACUP STUDY WEEK OF DEATH: 14 PROSECTOR: DOUGLAS HERNOON DOSE GROUP: 2 STUDY DAY OF DEATH: 95 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL DATE AND TIME OF NECROPSY: 07/14/86 14:46 SEX: MALE DATE OF DEATH: 07/14/86 ANIMAL NUMBER: B08410

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

CLINICAL OBSERVATIONS

-APPEARED NORMAL

-NEPHROPATHY, CHRONIC PROGRESSIVE,--FOCI OF MONONICLEAR CELLS, -MINIMAL HISTOPATHOLOGY > UNREMARKABLE KIDNEY (KD): LIUER (LT): HINIMA MINIMA OBSERUATIONS -ELECTRON MICROSCOPY SAMPLE; LIVER -GLOBE RUPTURED POST MORTEM; LEFT >NOTE:>EXTERNAL DBSERUATIONS:NOME GENERAL INFORMATION (XX): NECROPSY COLLECTED/TAKEN (XW) : PATHOLOGY EYE (EY) :

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRIA, THORACIC (AD), BINE, FEMUR (FE), BDNE, STERNUM (SB),
BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
BUDDENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXO (ED),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GL (SG),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI),
PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS), SPLFEN (SP), STOMACH, GL (ST),
STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UR) THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

-PERIBRONCHIAL/PERIUASCULAR, INFILTRATION, LYMPHOIO,-SL)GHT

> THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: LACRIMAL GL, EXO (EO)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTINCIAL) WERE SAVED ***

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/10X SYSTEM OUTPUT *** APPENDIX 8

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INDIVIDUAL ANIMAL SUMMARY REPORT

STHDY NUMBER: 2399108

TERMINAL BODY WEIGHT: 575.0 GRAMS RECORDER: SID JONES, DUM, PHD, DACUP SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE PATHOLOGIST: SID JONES, DUM, PHD, DACUP STUDY WEEK OF DEATH: 14 PROSECTOR: BARBARA DAY DOSE GROUP: 2 OF DEATH: 07/15/86 STUDY DAY OF DEATH: 96 AND TIME OF NECROPSY: 07/15/86 9:03 PROSE POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL DATE OF DEATH: 07/15/86 ANIMAL NUMBER: B08411

WEIGHER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO DRGAN WEIGHTS RECORDED ***

CLINICAL OBSERVATIONS

-RIGHT EYE-CHROMODACRYORRHEA;

MALCCCLUSION

PATHOLOGY OBSERVATIONS NECROPSY

-ELECTRON MICROSCOPY SAMPLE; LIVER GENERAL INFORMATION (XX) : *COLLECTED/TAKEN (XW) :

INFILTRATION, LYMPHOID, -SLIGHT

- PERTBROWCHIAL / PERTUASCULAR

LUNG (LU) :

HISTOPATHOLOGY

>NOTE:>EXTERNAL DASERVATIONS:RIGHT EYE-CHROMODACRYDRRHEA, MALDCCLUSION

THE FOLLOWING ORGANS WERE UNREPARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRIA, THORACIC (AD), BONE, FEMIR (FE), BONE, STERNUM (SB),
BRAIN WASTEM (BR), CECUM (CD), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
BUODENUM (DU), EPIDIDENUM (EP), ESCHAGUS (ES), EYE (EY), HEART (HT), ILEUM (LL), JECHNUM (AE), KIDNEY (KD),
LACRIMAL GL, EXO (ED), LIVER (LI), LN, MESENTERIC (MS), LN, DTHER (LN), LUNG (LI), MAMMARY GLAND (MS),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PARCREAS (FA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), TRACHEA (TR), URINARY BLADDER (UB)

FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: KIDNEY (KD), LIUER (LI) 뽀

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STIMY PROTOCOL) WERE SAVED ***

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/TOX SYSTEM OUTPUT *** APPENDIX 8

PRINTED: 12-MAY-88

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

HINAL BODY WEIGHT: 527.4 GRAMS RECORDER: SID JOHES, DUM, PHD, DACUP WEIGHER: NOT REQUIRED BY PROTOCOL SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE TERMINAL BODY WEIGHT: PATHOLOGIST: SID JONES, DUM, PHD, DACUP STUDY WEEK OF DEATH: 14 PROSECTOR: BARBARA DAY DOSE GROUP: 2 STUDY DAY OF DEATH: 96 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL AND TIME OF NECROPSY: 07/15/86 10:02 SEX: MALE DATE OF DEATH: 07/15/86 ANIMAL NUMBER: B08412

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

HISTOPATHOLOGY OBSERUATIONS NECROPSY PATHOLOGY CLINICAL OBSERVATIONS

-ELECTRON MICROSCOPY SAMPLE; LIVER >NOTE:>EXTERNAL OBSERVATIONS:NOME GENERAL INFORMATION (XX) : ^COLLECTED/TAKEN (XW) :

INFILTRATION, LYMPHOID, - SLIGHT -PERTBRONCHIAL / PERTUASCULAR THE CLU:

-NEPHROPATHY, CHRONIC PROGRESSIVE,-

MINIM

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRTA, THORACIC (AD), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THURACIC (TC),
DUDDENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUMS (LU), MAMMARY GLARD (MG),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, DIHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR), THE FOLLOWING ORGANS WERE UNREMARKABLE AT MECROPSY: URINARY BLADDER (UB)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: LIVER (LI) *** ALL ORGANS/TISSUES (REDUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

APPENDIX 8 *** PATH/TOX SYSTEM CUIPUT *** SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88

STUDY MUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE F DEATH: 14 TERMINAL BODY WEIGHT: 506.0 GRAMS RECORDER: SID JONES, DUM, PHD, DACUP ;, DUM, PHD, DACUP WEIGHER: TIM GROVE	SPAIN ORGAN STATUS	20 MEIGHT TOKEN	THE LEHT	THE TENT	APTONE TOKEN		нгэторатногосу	LUNG (LJ): -PERIBRONCHIAL/PERIVASCULAR, INFILTRATION, LYMPHOID,-MINIMAL
SCHE TERM	ORGAN TO BRAIN MEIGHT RATIO	.0270	1.000	.353	1,343	2.368	0 X C	TUNNS -
DOSE GROUP: 2 SACRIFICE STATUS: 197 STUDY WEEK OF DEATH: 14 PROSECTOR: TIM GROUE PATHOLOGIST: SIO JONES, DUM, PHD, DACUP	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	.0109	, 48.5 % , 25.7 %	.142 %	.542 %	2.468 % 955 %	THOLOGY, OBSERUATIONS NECROPSY	GENERAL INFORMATION (XX) : >NOTE:>EXTERNAL OBSERUATIONS:MONE
рентн	ABSOLUTE ORGAN WEIGHT (GRAMS)	.055	2.04	.72	2.74	12.49	€	GENERAL INF
ANIMAL NUMBER: 808413 SEX: MALE DATE OF DEATH: 07/16/86 STUDY DAY OF DATE AND TIME OF NECROPSY: 07/16/96 8:20 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL	DRGAN NAME	ADRENAL (AD)	BRAIN W/STEM (BR)	SPLEEN (SP)	KIDNEY (KD)	LIUER (LI) TESTIS/EPIDID (TP)	CLINICAL OBSERVATIONS	-APPEARED NORMAL

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AD), BONE, FEMIR (FE), BONE, STERNIM (SB),

BRAIN W.STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),

BRAIN W.STEM (BR), CECUM (CE), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILFIM (IL), DEJUNIM (JE), KIDHEY (KD),

LACRIMAL GL, EXD (ED), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG),

MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERUE, SCIATIC (SN), PANCREAS (FA),

PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS),

SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMIS (TH), THYROID (TY), TRACHEA (TR),

URINARY BLADDER (UB), *COLLECTED/TÁKEN (XW)

HE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: KIDNEY (KD), LIVER (LI)

^{***} ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WIRE SAUED ***

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/TOX SYSTEM DUTPUT *** APPENDIX B

PRINTED: 12-MAY-88

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY HUMBER: 2399108

TERMINAL BODY WEIGHT: 528.3 GRAMS RECORDER: SID JONES, DUM, PHD, DACUP WEIGHER: NOT REQUIRED BY PRITOCOL SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE PATHOLOGIST: SID JONES, DUM, PHD, DACUP STUDY WEEK OF DEATH: 14 PROSECTOR: TIM GROVE DOSE GROUP: 2 DEATH: 96 DATE OF DEATH: 07/15/86 STUDY DAY OF DATE AND TIME OF NECROPSY: 07/15/86 11:19 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL SEX: MALE ANIMAL NUMBER: B08414

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

-NEPHROPATHY, CHRONIC PROGRESSIVE,-HISTOPATHOLOGY KIDNEY (KD) : MINIMA OBSERUATIONS -ELECTRON MICROSCOPY SAMPLE, LIVER >NOTE:> EXTERNAL DRSERVATIONS:NONE GENERAL INFORMATION (XX) : NECROPSY *COLLECTED/TAKEN (XW) : PATHOLOGY CLINICAL OBSERVATIONS -APPEARED NORMAL

INFILTRATION, LYMPHOID, -SLIGHT

-PERIBRONCHIAL/PERIUASCIALAR,

(T.E)

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AGRIA, THORAGIC (AD), ROWE, FEMUR (FE), BORNE, STERNUM (SB),
ADRENAL CORTEX (AC), ADRENAL, MEDULLA (CM), CORD, CERUICAL (CS), CORD, LUMBAR (LC), CORD, THORAGIC (TG),
BUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (LL), DERUNUM (DE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERUE, SCIATIC (SN), PANCREAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONIGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR), FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY: JRINARY BLADDER (UB) · 置

FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: LIVER (LI) 표

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STLIOY PROTOCOL) MERE SAVED ***

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/IDX SYSTEM DUTP(IT *** APPENDIX 8

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INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399188

SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE PATHOLOGIST: SID JONES, DUM, PHO, DACUP 4: 96 STUDY WEEK OF DEATH: 14 PROSECTOR: DOUGLAS HERNDON DOSE GROUP: 2 DEATH: 96 STUDY DAY OF POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL DATE AND TIME OF NECROPSY: 07/15/86 12:19 DATE OF DEATH: 07/15/86 NUMBER: B08415 ANI MAL

TERMINAL BODY WEIGHT: 460.6 GRAMS
RECORDER: SIO JONES, DUM, PHD, DACUP
WEIGHER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

CLINICAL OBSERVATIONS

-APPEARED NORMAL

OBSERVATIONS

-ELECTRON MICROSCHPY SAMPLE; LIUFR *COLLECTED/TAKEN (XW) :

>NOTE:>EXTERNAL DBSERVATIONS:NOWE GENERAL INFORMATION (XX):

INFILIRATION, LYMPHOLO, -SELIGHT -PERIBRONCHIAL/PERIUASCULAR

-NEPHROPATHY, CHRONIC PROGRESSIVE,-

KIDNEY (KD)

LING CLID : MINIMAL

HISTOPATHOLOGY

THE FOLLOWING ORGANS WERE UNREMARKABLE AT HECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AD), BONE, FEMUR (FE), BONE, STERNIM (SB),
BRAIN W.STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE),
LACRIMAL GL, EXO (ED), LIVER (LI), LN, MESENTFRIC (MS), LN, OTHER (LN), LING (LII), MAMMARY GLABO,
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERUE, SCIATIC (SN), PANCREAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL UESICLE (SV), SKIN (SK), SKIN, OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), TRACHEA (TR), URINARY BLADDER (UB)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: LIVER (L1) *** ALL ORGANS/TISSUES (REQUIRED TO BE MARVESTED PER THE STUDY PROTOCOL) MFRE SAUED ***

SUBCHRONIC TOXICITY STUDY IN RATS APPENDIX 8

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INDIVIDUAL ANIMAL SUMMARY REPORT

STHDY MIMBER: 2399108

TERMINAL BODY WEIGHT: 425.6 GRAMS RECTIRDER: JAMES CANNON SACRIFICE STATUS: UNSCHEDULED (D) PATHOLOGIST: NOT REQUIRED BY PROTOCOL STUDY WEEK OF DEATH: 5 PROSECTOR: TIM GRAUE DOSE GROUP: 2 DATE OF DEATH: 05/14/86 STUDY DAY OF DEATH: 34
DATE AND TIME OF NECROPSY: 05/14/86 11:57 PROSE POST-FIX WEIGHER: NOT REDUIRED BY PROTOCOL SEX: MALE ANIMAL NUMBER: B08416

WEIGHER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

 	PATHOLOGY OBSERVATIONS	
CLINICAL OBSERVATIONS	NECROPSY	HISTUPALHULUSY
-APPEARED NORMAL	BRAIN WYSTEM (BR) :	BRAIN M/STEM (BR) :
	-S0FT	> LINRE MARKAFILE
	LUNG (LU):	CECUM (CE) :
	-FAILURE TO COLLAPSE; ALL LOBES	VIISSUE MISSING
	GENERAL INFORMATION (XX):	COLLON (CO) :
	SNOTE: SLAST IN-LIFE AND EXTERNAL	VIISSIE MISSING
	DBSERVATIONS: NONE. FOUND DEAD	DUODENLIM (DU) :
•	BEFORE DOSING	>TISSUE MISSING
		ILEUM (II.) :
		>TISSUE MISSING
-		JEJUNUM CJE) ;

INFILTRATION, LYMPHOID, -SLIGHT -PERIBRONCHIAL/PERIVASCULAR, -FORETGN MATERIAL, - PRESENT

TISSUE MISSING

RECTUM (RE):

YTISSUE MISSING

1 (11) 54111

SUBCHRONIC TOXICITY STUDY IN RATS *** TRAING MBISKS XUL/HIDA *** APPENDIX B

PRINTED: 12-MAY-88 PAGE: 217

STUDY NUMBER: 23991118

INDIVIDUAL ANIMAL SUMMARY REPORT

TERMINAL BODY WEIGHT: 429 RECORDER: JAMES CANNON SACRIFICE STATUS: UNSCHEDULED (D) PATHOLOGIST: NOT REQUIRED BY PROTOCOL STUDY WEEK OF DEATH: 5 PROSECTOR: TIM GROVE DOSE GROUP: 2 STUDY DAY OF DEATH: 34 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL DATE AND TIME OF NECROPSY: 05/14/86 11:57 SEX: MALE DATE OF DEATH: 05/14/86 ANIMAL NUMBER: 808416

WEIGHER: NOT REQUIRED BY PROTOCOL

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRIA, THORACIC (AD), BOHE, FEMUR (FE), BOHE, STERNIM (SB), CECUM (CE), CORD, CORD, CORD, LUMBAR (LC), CORD, THORACIC (TC), DUGDENUM (DU), EPIDIDYMIS (EP), COLON (CO), CORD, CERVICAL (CS), HEART (HT), ILEUM (IL), JEJUNIM (JE), KIDNEY (KD), LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNIM (SE), MUSCLE, SKELETAL (SM), NERUE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PI), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NINGEL (SU), TRACHEA (TR), URINARY BLADDER (1B), "COLLECTED/TAKEN (XW) THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AD), BONE, FEMURE (FE), BONE, STERNUM (SB), CORD, CORD, LUMBAR (LC), CORD, THORACIC (TC), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), KIDNEY (KD), LACRIMAL GL, EXO (ED), LIVER (LT), LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), SEMINAL VESICLE (SU), SKIN (SK), SPLEEN (SP), STOMACH, RL (ST), STOMACH, HONGL (SU), TESTIS (TE), THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB)

*** ALL ORGANS/TISSUES (REDUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

*** PATH/TOX SYSTEM DUJTPUJT *** SUBCHRONIC TOXICITY STUDY IN RATS APPENDIX B

PRINTED: 12-MAY-80 PAISE: 218

STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

DOSE GROUP: 2 SAFRIFICE STATUS: UNSCHEDULED (D)
4: 15 STUDY WEEK OF DEATH: 3 TERMINAL BODY WE
PROSECTOR: JAMES CANNON
PATHOLOGIST: NOT REQUIRED BY PROTOCOL WEIGHER: NOT SEX: MALE DEATH: 15 DATE OF DEATH: 04/25/86 STUDY DAY OF DATE AND TIME OF NECROPSY: 04/25/86 14:35 NUMBER: B08417

WEIGHER: NOT REQUIRED BY PROTOCOL TERMINAL BODY WEIGHT: 309 RECARDER: JAMES CANNON

305.5 GRAMS

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL

ANIMAL

	Y O B S NECROPSY	į
-APPEARED NORMAL	BRAIN W/STEM (BR): -SOFT; FOREBRAIN LUNG (LU): -FAILURE TO COLLAPSE; ALL LOBES GENERAL INFORMATION (XX): >NOTE:>LAST IN-LIFE AND EXTERNAL OBSERVATIONS:CONVULSIONS, FOUND OEAD	ADREMAL, MEDULLA (AM): -UNILATERALLY EXAMINED,-PRESENT AORTA, THORACLY (AD): >TISSUE MISSING BRAIN W/STEM (BR): >UNREMARKABLE LUNG (LU): -PERIBRONCHIAL/PERIUASCULAR, INFILTRATION, LYMPHOTO,-SLIGHT -FOREIGN MATERIAL,-PRESENT MAMMARY GLAND (MG): >SECTION EXAMINED; TISSUE NOT PRESENT NERU, SCIATISCUS (SN): >TISSUE MISSING PROSTATE (PR): -MOMMINGERR CELL INFILTRATE,-SLIGHT

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/TOX SYSTEM DUTPUT *** APPENDIX B

PRINTED: 12-MAY-88

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

WEIGHER: NOT REQUIRED BY PRITOCIN 315.5 GRAMS RECORDER: JAMES CANNON TERMINAL BODY WEIGHT: SACRIFICE STATUS: UNSCHEDULED (D) PATHOLOGIST: NOT REQUIRED BY PROTOCOL STUDY WEEK OF DEATH: 3 PROSECTUR: JAMES CANNON DOSE GROUP: 2 STUDY DAY OF DEATH: 15 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL AND TIME OF NECROPSY: 04/25/86 14:35 SEX: MALE DATE OF DEATH: 04/25/86 ANIMAL NUMBER: B08417

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRIA, THORACIC (AD), BONE, FEMINR (FE), ROME, STERFULM (SB), GETLUM (CE), CORD, CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC), DUBODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MARROW, STENUM (SE), MARROW, STOMACH, GL, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), PRUSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NUNSL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UR), ^COLLECTED/TAKEN (XW)

(88) ADRENAL, CORTEX (AC), BONE, FEMUR (FE), BONE, STERNIM (SB), CECUM (CE), COLON (CD), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC), DUDDENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXO (ED), LIVER (LI), LN, MESENTERIC (MS), MAND SALIDARY GL MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), RECTUM (RE), SEMINAL UESICLE (SU), SKIN (SK), SPLEEN (SP), STOMACH, GL (ST), STOMACH, GL (SI), TESTIS (TE), THYMUS (JH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB) FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: IHE

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

SUBCHRONIC TOXICITY STUDY IN RATS APPENDIX 8 *** PATH/IOX SYSTEM OUTPUT ***

PRINTED: 12-MAY-88 PAGE: 220

STUDY HUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

DULED, TERMINAL SACRIFICE INAL BODY WEIGHT: 225.9 GRAMS RECORDER: SID JONES, DUM, PHD, DACUP WEIGHER: TIM GROVE	ORGAN STATUS	0244 WEIGHT TAKEN 000 WEIGHT TAKEN 620 WEIGHT TAKEN 549 WEIGHT TAKEN 649 WEIGHT TAKEN 640 W	INFILIRATION, I YMPHIIO, -SLIGHT
SCHE	ORSAN TO BRAIN WEIGHT RATIO		INFLLTRATIO
WEEK O SRCYJE D JONES	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	50	F 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
F DEATH	ABSOLUTE ORGAN WEIGHT (GRAMS)	2.05 2.05 1.27 .74 3.38 13.30 4.90 P A T H O L C GENERAL INFOR	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
ANIMAL NUMBER: B08418 SEX; MALE DATE OF DEATH: 07/16/86 STUDY DAY OF DATE AND TIME OF NECROPSY: 07/16/86 11:24 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL	ORGAN NAME	ADRENAL (AD) BRAIN W/STEM (BR) HEART (HT) SPLEEN (SP) KIDNEY (KD) LIVER (L1) TESTIS/EPIDID (TP) CLINICAL OBSERVATIONS -APPEARED NORMAL	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), THORAGIC (AG), BONE, FEMIR (FE), BOME, SIFRRUM (SB),
BADRENAL CORTEX (AC), ADRENAL, MEDULLA (CA), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
BUODDENUM (DU), EPIDIDYMIS (EP), ESCHAGUS (ES), FYE (EY), HEART (HI), ILEMA (LU), MAMMARY GLAND (MG),
LACRIMAL GL, EXD (EO), LIVER (LI), LN, MESENTERIC (MS), LN, DTHER (LN), LUNG (LU), MAMMARY GLAND (MG),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MISCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (FA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SU), SKIN (SK), SKIN, OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMIS (TH), THYROID (TY), TRACHER (TR),
URINARY BLADDER (UB), ACOLLECTED/TAKEN (XW)

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: LIVER (L1) 포

^{***} ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/IOX SYSTEM OUTPUT *** APPENDIX 8

PRINTED: 12-MAY-BR

STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

TERMINAL BODY WEIGHT: 499.3 GRAMS RECORDER: SID JONES, DUM, PHD, DACUP SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE

4: 97 STUDY WEEK OF DEATH: 14 PROSECTOR: DOUGLAS HERNDON DOSE GROUP: 2 STUDY DAY OF DEATH: 97 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL DATE AND TIME OF NECROPSY: 07/16/86 10:03 DATE OF DEATH: 07/16/86 ANIMAL NUMBER: 808419

WEIGHER: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHO, DACUP

HISTOPATHOLOGY

CLINICAL DBSERUATIONS

-APPEARED NORMAL

*** ANIMAL HAS NO DRGAN WEIGHTS RECORDED ***

PATHOLOGY OBSERVATIONS NECROPSY

^COLLECTED/TAKEN (XW) :
 -ELECTRON MICROSCOPY SAMPLE; LIVER >NOTE:>EXTERNAL OBSERVATIONS:NONE GENERAL INFORMATION (XX):

1

INFILTRATION, LYMPHOID, -SLIGHT -PERTBROWCHIAL/PERTUASCULAR LUMBS (LU) :

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRIA, THORACIC (AD), BONE, FEMUR (FE), BONE, STERNUM (SB), BRAIN W/STEM (BR), CECUM (CC), CORD, CRUICAL (CS), CHRD, LUMBAR (LC), CORD, THORACIC (TC), DUDDENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), MARMARY GLAND (MS), MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA), PARRATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL UESICLE (SU), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR), THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY: URINARY BLADDER (UB)

FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: KIDNEY (KD), LIVER (LI) 뿔

*** ALL DRGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

APPENDIX B *** PATH/TÜX SYSTEM OUTPUT *** SUBCHRÖNIC TÖXICITY STUDY IN RATS

PRINTED: 12-MAY-88 PAGE: 222

STUDY HUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: 808420 SEX: MALE DATE OF DEATH: 07/16/86 STUDY DAY OF OATE AND TIME OF NECROPSY: 07/16/86 14:10 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL	F DEATH:	DOSE GROUP: 2 SACRIFICE STATUS: 1: 97 STUDY WEEK OF DEATH: 14 PROSECTOR: DOUGLAS HERNDON PHO, DACUP PATHOLOGIST: SID JONES, DUM, PHO, DACUP	SCHE	DULED, TERMINAL SACRIFICE final BODY WEIGHT: 443.2 GRAMS RECORDER: SID JONES, DUM, PHD, DACUP WEIGHER: DOUGLAS HERNOOM
ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO RODY WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO	ORGAN STATUS
ADRENAL (AD) BRAIN W.STEM (BR) HEART (HT) SPLEEN (SP) KIDNEY (KD) LIUGR (LI) TESTIS/EPIDID (TP)	2.19 1.36 1.36 2.71 10.94 5.91	. 0109 x . 4993 x . 308 x . 170 x . 611 x . 2468 x . 1 . 34 x . 3	1.000 .624 .344 1.239 5.005	WEIGHT TAKEN WEIGHT TAKEN WEIGHT TAKEN WEIGHT TAKEN WEIGHT TAKEN WEIGHT TAKEN
CLINICAL OBSERVATIONS		OGY OBSERUATI	8 Z O	HISTOPATHOLOGY
-MALOCCLUSION	GENERAL INFORMATION > NOTE:> EXTERNAL OBSERVATION	NFORMATION (XX): EXTERNAL OBSERVATIONS: MALOCCLUSION	KIDNEY (KD) -NEPHROPATH MINIMAL -CORTICAL C' LIUER (LI) : -FOCI OF MOI LIMS (LU) : -PERIBRONCH	DNEY (KD): -NEPHROPATHY, CHRONIC PROGRESSIVE,- MINIMAL -CORTICAL CYST,-PRESENT UER (L.1): -FOCI OF MONONJOLEAR CELLS,-MINIMAL NS (L.0): -PERIBRONCHIAL/PERIVASCULAR, INFILTRATION, LYMPHOID,-MINIMAL
THE FOLLOWING ORGANS WERE	THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	1 1 1	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ANRIA, THORACIC (AN), BONE, FENIS (FE), BONE, STERRUM (SB),
BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUDDENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIUNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LING (LU), MAMMARY GLAND (MS),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERUE, SCIATIC (SN), PANCREAS (PA),
PARATHYROID (PT), PITULTARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHFA (TR),
URINARY BLADDER (UB), ACOLLECTED/TAKEN (XW)

^{***} ALL ORGANS/TISSUES (REQUIRED TO BE MARVESTED PER THE STUDY PROTOTOL) MERE SAVED ***

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/TDX SYSTEM DUTPUT *** APPENDIX 8

PRINTED: 12-MAY-88 PAGE: 223

INDIVIDUAL ANIMAL SÜMMARY REPORT

STUDY NUMBER: 2399108

TERMINAL BODY WEIGHT: 414.5 GRAMS RECORDER: SIO JONES, DUM, PHD, DACUP WEIGHER: NOT REQUIRED BY PROTOCOL SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE PATHOLOGIST: SID JONES, DUM, PHD, DACUP STUDY WEEK OF DEATH: 14 PROSECTOR: DOUGLAS HERNDON DOSE GROUP: 2 DEATH: 97 STUDY DAY OF POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL 8:45 SEX: MALE DATE AND TIME OF NECROPSY: 07/16/86 DATE OF DEATH: 07/16/86 NUMBER: 808421 ANIMAL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

CLINICAL DBSERVATIONS

-APPEARED NORMAL

PATHOLOGY OBSERVATIONS NECROPSY

-ELECTRON MICROSCOPY SAMPLE; LIVER GENERAL INFORMATION (XX): *COLLECTED/TAKEN (XW) :

YNDTE:>EXTERNAL OBSERVATIONS:NONE

-NFFHROPATHY, CHRONIC PROGRESSIVE,-INFILTRATION, LYMPHOID, - SLIGHT -PERIBRONCHIAL/PERIUASCULAR, KIDNEY (KD): (LU) St. IGHT _ | |}

HISTOPATHOLOGY

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AD), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W.STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUGOENUM (DU), EPIDIOYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEARI (HI), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUMS (LU), MAMMORY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), RECTUM (RE), SEMINAL VESICLE (SU), SKIN (SK), SKIN, OTHER (SS),
SPLEEN (SP), STOMACH, GL (SI), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR), THE FOLLOWING DRGANS WERE UNREMARKABLE AT NECROPSY: URINARY BLADDER (UB)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: LIVER (L1) *** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAUFD ***

APPENDIX B *** PATH/IOX SYSTEM OUTPUT *** SUBCHRONIC TOXICITY STIJOY IN RATS

PRINTED: 12-MAY-88 PACE: 224

INDIVIDUAL ANIMAL SUMMARY REPORT

PAGE: 224

STUDY NIMBER: 2399108

DOSE GROUP: 3 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE TH: 95 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 452.4 GRAMS PROSECTOR: BARBARA DAY PATHOLOGIST: SID JONES, DUM, PHD, DACUP WEIGHER: NOT REQUIRED BY PROTOCOL	*	3 HISTOPATHOLOGY
	*	į .
ANIMAL NUMBER: 808442 SEX: MALE DATE OF DEATH: 02/14/86 STUDY DAY OF DEA DATE AND TIME OF NECROPSY: 02/14/86 9:39 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL	*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED **	CLINICAL

-NEPHROPATHY, CHRONIC PROGRESSIVE,-

KIDNEY (KD):

-ELECTRON MICROSCOPY SAMPLE; LIVER

*COLLECTED/TAKEN (XW) :

-APPEARED NORMAL

NOTE: > EXTERMAL GRSERUATIONS: NONE

GENERAL INFORMATION (XX) :

INFILTRATION, LYMPHOID, -SLIGHT

-PERIBRONCHIAL/PERIUASCULAR

MINIMAL LUNS (LU) :

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ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ANRIA, THORACIC (AD), EDNE, FEMIR (FE), BOHE, STERNIM (SB),
BRAIN WASTEM (BR), CECUM (CE), COLON (CD), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUDDENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JF), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, DTHER (LN), LUNG (LU), MAMMARY GLAND (MG),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MISCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (FA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, DTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, MINGL (SU), TESTIS (IE), THYMUS (IH), THYROID (TY), TRACHFA (TR), URINARY BLADDER (UB)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/TOX SYSTEM QUITPLIT *** APPENDIX 8

PRINTED: 12-MAY-88

STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

IINAL BODY WEIGHT: 481.1 GRAMS RECORDER: SID JONES, DUM, PHD, DACUP WEIGHER: NOT REQUIRED BY PROTOCOL SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE DF DEATH: 14 TERMINAL BODY WEIGHT: 481.1 PATHOLOGIST: SID JONES, DUM, PHO, DACUP STUDY WEEK OF DEATH: 14 PROSECTOR: DOUGLAS HERNDON DOSE GROUP: 3 DEATH: 95 STUDY, DAY OF POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL 07/14/86 10:50 SEX: MALE AND TIME OF NECROPSY: DATE OF DEATH: 07/14/86 ANIMAL NUMBER: B08443

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

PATHOLOGY OBSERVATIONS NECROPSY CLINICAL OBSERVATIONS

-DARK AREA; DNE, DARK RED, 1.0 X 0.5 (PR) : PROSTATE

-APPEARED NORMAL

INFILTRATION, LYMPHOID, -SLIGHT

PROSTATE (PR): > UNREMARKABLE

-PERTERCINCHTAL/PERTUASIULAR

CUNG CLUB:

HISTOPATHOLOGY

YNDTE: YDARK AREA, POSSIBLE INJECTION

^COLLECTED/TAKEN (XW) : -ELECTRON MICROSCOPY SAMPLE; LIVER >NOTE:>EXTERNAL OBSERVATIONS:NONE GENERAL INFORMATION (XX) :

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRIA, THORACIC (AD), BDNE, FEMUR (FE), BDNE, STERNIM (SB),
BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORD, CORD, CORD, LUMBAR (CC), CORD, THURACIC (TC),
BUDDDENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIONEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LING (LU), MAMMARY GLARD,
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA),
PARATHYROID (PT), PITUITARY (PI), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS), SPLEFN (SP),
STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB) THE FOLLOWING DRGANS WERE UNREMARKABLE AT NECROPSY:

FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: KIDNEY (KD), LIVER (LI) 품

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

APPENDIX.8 *** PATH/TOX SYSTEM CUIPUT *** SUBCHRONIC TOXICITY STIDY IN RATS

PRINTED: 12-MAY-88 PAGE: 226

INDIVIDUAL ANIMAL SUMMARY REPORT

23991 NR	
NUMBER	
STUDY	

ANIMAL NUMBER: B08444 SEX: MALE DATE OF DEATH: 07/14/86 STUDY DAY OF DATE AND TIME OF NECROPSY: 07/14/86 8:45 POST-FIX WEIGHER: NOT REGUIRED BY PROTOCOL	. БЕАТН	DOSE GROUP: 3 SACRIFICE STATUS: 1: 95 STUDY WEEK OF DEATH: 14 PROSECTOR: DOUGLAS HERNDON PATHOLOGIST: SID JONES, DUM, PHD, DACUP	SCHE	SCHEDULED, TERMINAL SACRIFICE TERMINAL BODY WEIGHT: 500.0 GRAMS RECHROER: SID JONES, DUM, PHD, DACUP WEIGHER: DOUGLAS HERNDON
ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO	ORGAN Status
ADRENAL (AD) BRAIN W/STEM (BR)	. 042	.0084 % .464 %	. n181 . n000	i i i
HEART (HT) SPLEEN (SP)	1.22	. 160 % % % % % % % % % % % % % % % % % % %	. 526 . 345 . 45	WEIGHT TAKEN WEIGHT TAKEN
LIVER (LI) TESTIS/EPIDID (TP)	13.50 5.38	2,700 % 1,076 %	5.819 2.319	
CLINICAL OBSERVATIONS		ATHOLOGY OBSERUATIONS NECROPSY	S Z O	HISTOPATHOLOGY
- APPEARED NORMAL	GENERAL INFO	GENERAL INFORMATION (XX): >MOTE:>EXTERNAL (BSSERVATIONS: NONE	KIONEY (KD) 1 - NEPHROPATHY SLIGHT LING (1:1) : - PERIBRONCHI INFILTRATIO	ONEY (KD): -NEPHROPATHY, CHRONIC PROGRESSIVE,- SLIGHT NG (14): -PERIBRONCHIAL/PERIVOSCULAR, INFILTRATION, LYMPHOID,-SLIGHT
THE FOLLOWING ORGANS WERE UNREMARKABLE AT	NREMARKABLE AT NECROPSY:	1	1 1 1	; ; ; ; ;

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRIA, THORACIC (AD), BONE, FEMUR (FE), BONE, STERNUR (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNIM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MS),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERUE, SCIATIC (SN), PANCREAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SU), SKIN (SK), SKIN, OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHFA (TR),

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCHPIC EXAMINATION:

^{***} ALL ORGANS/IISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) LAFRE SAVED ***

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/10X SYSTEM DUITPUT *** APPENDIX 8

PRINTED: 12-MAY-88 PAISE: 227

STUDY NUMBER: 2399188

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY WEEK OF DEATH: 14 DOSE GROUP: 3 DEATH: 95 ANIMAL NUMBER: B08445

SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
IF DEATH: 14 TERMINAL BODY WEIGHT: 455.1 GRANS
A RECORDER: SID JONES, DUM, PHD, DACUP
A REIGHFR: MIT REQUIRED BY PROTOCOL

PATHOLNEIST: SID JONES, DUM, PHD, DACUP PROSECTOR: BARBARA DAY DATE OF DEATH: 02/14/86 STUDY DAY DF DATE AND TIME OF NECROPSY: 02/14/86 12:00 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

CLINICAL OBSERVATIONS

-APPEARED NORMAL

PATHOLOGY OBSERVATION NECROPSY

COLLECTED/TAKEN (XW) : -ELECTRON MICROSCOPY SAMPLE; LIUER >NOTE:>EXTERNAL DBSERVATIONS:NONE GENERAL INFORMATION (XX):

INFILTRATION, LYMPHOID, -SLIGHT

-PERIBRONCHIAL/PERIUASCULAR,

: (n'1) :

HISTOPATHOLOGY

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX. (AC), ADRENAL, MEDULLA (AM), ADRIA, THORAGIC (AD), BINNE, FEMUR (FE), BONE, STERNUM (SA),

BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),

BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORD, CRVICAL (CS), LM HEART (HT), ILEUM (IL), JESUMUM (JE), KIDNEY (KD),

LACKIMAL GL, EXO (ED), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LING (IU), MAMMARY GLAND (MS),

MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERUE, SCIATIC (SN), PANGREAS (PA),

PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICIE (SV), SKIN (SK), SKIN, OTHER (SS),

SPLEEN (SP), STOMACH, GL (SI), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR),

FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: KIDNEY (KD), LIVER (LI) 뽀

*** ALL DRGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

A** PATH/TOX SYSTEM OLITPLIT *** SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88 PAGE: 228

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

TERMINAL BODY WEIGHT: 316.7 GRAMS
RECORDER: BARBARA DAY
WEIGHER: NOT REQUIRED BY PROTOCOL SACRIFICE STATUS: UNSCHEDULED (D) 4: 20 STUDY WEEK OF DEATH: 3
PROSECTOR: BARBARA DAY
PATHOLOGIST: NOT REQUIRED BY PROTOCOL DOSE GROUP: 3 ANIMAL NUMBER: B08446 SEX: MALE DOS
DATE OF DEATH: 04/30/86 STUDY DAY OF DEATH: 20
DATE AND TIME OF NECROPSY: 04/30/86 15:50 PROSE
POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL PATHO

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

CLINICAL OBSERVATIONS	ATHOLOGY OBSERVATION NECROPSY	HISTOPA
-APPEARED NORMAL	LUNG (LU): -FAILURE TO COLLAPSE; ALL LOBES -MOTTLED; ALL LOBES, LIGHT TO DARK RED GENERAL INFORMATION (XX): >NOTE:>LAST IN-LIFE AND EXTERNAL DBSERVATIONS:NONE, DIED SHORTLY AFTER DOSING	LUNG (LU): -PERIBRONCHIAL/PFRIVASCULAR, INFILTRATION, LYMPHOID,-MINIMAL PARATHYROID (PT): >TISSUE MISSING PROSTATE (PR): -MONONJCLEAR CELL INFILTRATE,-SLIGHT THYROID (TY): >TISSUE MISSING

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/TOX SYSTEM DUTPUT *** APPENDIX 8

PRINTED: 12-MAY-88 PAGE: 279

STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

WEIGHER: NOT REQUIRED BY PRUTOCOL 316.7 GRAMS RECORDER: BARBARA DAY TERMINAL BODY WEIGHT: SACRIFICE STATUS: UNSCHEDULED (D) PATHOLOGIST: NOT REQUIRED BY PROTOCOL STUDY WEEK OF DEATH: 3 PROSECTOR: BARBARA DAY DOSE GROUP: 3 STUDY DAY OF DEATH: 20 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL DATE AND TIME OF NECROPSY: 04/30/86 15:50 SEX: MALE DATE OF DEATH: 04/30/86 ANIMAL NUMBER: 808446

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRIA, THORACIC (AD), BUNE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN W.STEM (BR), CECUM (CE), CORD, CORD, CORD, CORD, LUMBAR (LC), CORD, THORACIC (TC),
BUDDENUM (DU), EPIDIOYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (RD),
LACRIMAL GL, EXO (ED), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), MANMARY GLAND (MS), MAND SALIVARY GL (SG),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PT), PITITTARY (PI),
PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST),
STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY READDER (18), ACOLLECTED/TAKEN (XM)

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AN), ADRIA, THORAGIC (AD), RONE, FEMIR (FE), BONE, STERNIM (SB), ADRENAL, CORTEX (AC), ADRENAL (CS), CORD, LUMBAR (LC), CORD, THORAGIC (TC), DUDDENUM (DU), EPIDIOVINIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILENIM (IL), DEJUNUM (DE), KIDHEY (KD), LACRIMAL GL, EXD (EO), LIVER (LI), LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MASCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA), PITIITARY (PI), RECTUM (RE), SEMINAL VESICLE (SU), SKIN (SK), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMIS (TH), TRACHEA (TR), URINARY BLADDER (UB) FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: 포

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) MERE SAVED ***

SHBCHRONIC TOXICITY STUDY IN RATS *** PATH/TOX SYSTEM DUTPUT *** APPENDIX B

PRINTED: 12-MAY-88 PAGE: 230

STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

SACRIFICE STATUS: SCHEDULEO, TERMINAL SACRIFICE
DF DEATH: 14 TERMINAL BODY WEIGHT: 468.5 GRAMS
RNDON
S, DVM, PHD, DACUP WEIGHFR! NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DACUP STUDY WEEK OF DEATH: 14 PROSECTOR: DOUGLAS HERNDON DOSE GROUP: 3 STUDY DAY OF DEATH: 96 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL DATE AND TIME OF NECROPSY: 07/15/86 8:49 SEX: MALE DATE OF DEATH: 07/15/86 ANIMAL NUMBER: B08447

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

-MEPHROPATHY, CHRONIC PROGRESSIVE,--FREI OF MONORMELEAR CELLS,-MINIMAL THE IL TRATION, LYMPHOLD, - SLIGHT -PERTBRONCHTAL/PERTUASCIALAR HISTOPATHOLOGY -PYELONEPHRITIS, -SLIGHT KIDNEY (KD) : (L.D.: CUNG (LU) : MINIMAL OBSERUATIONS -ELECTRON MICROSCOPY SAMPLE, LIVER OBSERVATIONS: MALOCCLUSION GENERAL INFORMATION (XX) : NECROPSY COLLECTED/TAKEN (XW) : PATHOLOGY NOTE: SEXTERNAL CLINICAL OBSERVATIONS -MALOCCLUSION

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THÜRACIC (AD), BONE, FEMUR (FE), BONE, STERNUM (SB),

BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORD, CERVIGAL (CS), CORD, LIMBAR (LC), CORD, THORACIC (TC),

DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),

LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUMG (LI), MAMMARY GL AHD (MS),

MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERUE, SCIATIC (SN), PANGREAS (PA),

PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SU), SKIN (SK), SKIN, OTHER (SS),

SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHÉRA (TR), JRINARY BLADDER (UB)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PRITHING) WERE SAVED ***

*** PATH/TOX SYSTEM OUTPUT *** SUBCHRONIC TOXICITY STRDY IN RAIS APPENDIX 8

PRINTED: 12-MAY-8B PAGE: 231

STIJDY NUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

SACRIFICE STATUS: UNSCHEDULED (D) PATHOLOGIST: NOT REQUIRED BY PROTOCOL I: 34 STUDY MEEK OF DEATH: 5 PROSECTOR: BARBARA DAY DOSE GROUP: 3 STUDY DAY OF DEATH: 34 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL DATE OF DEATH: 05/14/86 STUDY DAY OF DATE AND TIME OF NECROPSY: 05/14/86 12:05 SEX: MALE ANIMAL NUMBER: B08448

WETCHER: NOT REDUINED BY PROTOCOL TERMINAL BODY WEIGHT: 363 RECORDER: JAMES CANNON

HISTOPATHOLOGY

362.4 GRAMS

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

CLINICAL DBSERVATIONS

-APPEARED NORMAL

BRAIN W/STEM (BR) : > JFIRE MARKABLE DUDDENUM (DID ILEUM (IL) : (CE) : CO NO TOO > AUTOLYTIC >AUTOLYTIC MITTELYTIC) ALITTIL YT IC CECUM PATHOLOGY OBSERUATIONS -MOTTLED; ALL LOBES, LIGHT TO DARK RED DBSERVATIONS: NONE, FOUND DEAD ALL LOBES ENERAL INFORMATION (XX) : >NOTE:>LAST IN-LIFE AND EXTERNAL NECROPSY -FAILURE TO COLLAPSE: BEFORE DOSING GENERAL INFORMATION BRAIN WASTEM (BR) : CONS (CC) :

SECTION EXAMINED, TISSUE NOT PRESENT -FIRETON MATERIAL, -PRESENT MAMMARY GLAND (MG) RECTUM (RE) : > PUTOLYTIC CINE (CI):

DECIUMINA COED a

> AUTOLYTIC

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/IDX SYSTEM DUTPUT *** APPENDIX B

PRINTED: 12-MAY-88

INDIVIDIDAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

RECORDER: JAMES CANNON TERMINAL BODY WEIGHT: SADRIFICE STATUS: UNSCHEDULFD (D) PATHOLOGIST: NOT REQUIRED BY PROTOCOL STUDY WEEK OF DEATH: 5 PROSECTOR: BARBARA DAY DOSE GROUP: 3 DATE OF DEATH: 05/14/86 STUDY DAY OF DEATH: 34
DATE AND TIME OF NECROPSY: 05/14/86 12:05
POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL PATHC SEX: MALE ANIMAL NUMBER: B08448

WEIGHER: NOT REQUIRED BY PROTOCOL

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRIA, THURACIC (AD), BONE, FEMINE (FE), BONE, STERNIM (SB), CFCLM (CE), COLON (CO), CORO, CERVICAL (CS), CORO, LUMBAR (LC), CORO, THORACIC (TC), DUODENUM (DU), EPIDIDYMIS (EP), COLON (CO), CORO, CERVICAL (CS), LAGART (HI), ILEUM (IL), REJUNUM (JE), KIDNEY (KD), LACRIMAL SL, EXO (ED), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNIM (SE), MARROW (SE), MARROW (SE), NERLETAL (SM), NERUE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PI), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL UESICLE (SU), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONISL (SI), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (1B), ^COLLECTED/TAKEN (XW) THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRIA, THORACIC (AD), BONE, FEMUR (FE), BONE, STERNUM (SB), CORD, LUMBAR (LC), CORD, THORACIC (TC), EPIDIDYMIS (EP), ESOPHABUS (ES), EYE (EY), HEART (HT), KIDNEY (KD), LACRIMAL GL, EXD (ED), LIVER (LI), IN, MESENTERIC (MS), MAND SALIVARY (AL (SS), MARRIM, STERNUM (SE), MUSCLE, SKELETAL (SM), NERUE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), SEMINAL UESICLE (SU), SKIN (SK), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NOWEL (SM), TESTIS (TF), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB) THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

APPENDIX 8 *** PATH/IDX SYSTFM (NUTPLIT *** SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88 PAGE: 233

STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: B08449 SEX: MALE DATE OF DEATH: 07/14/86 STUDY DAY OF DATE AND TIME OF NECROPSY: 07/14/86 11:35 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL	SEX: MALE DOSE STUDY DAY OF DEATH: 95 17/14/86 11:35 PROSEC RED BY PROTOCOL PATHOL	DOSE GROUP: 3 H: 95 STUDY WEEK PROSECTOR: 11M GROUE PATHOLOGIST: SID JOH	_ vi	SCHE	SCHEDULED, TERMINAL SACRIFICE TERMINAL BODY WEIGHT: 423.1 GRAMS RECORDER: SID JONES, DUM, PHD, DACUP WEIGHER: TIM GROUE
ORGAN NAME	ABSOLUTE ORGAN (GRAMS)	WEIGHT	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN JEIGHT RATIO	ORGAN STATUS
ADRENAL (AD)	. 044	!	.01115 %	. 0227	WEIGHT TAKEN
BRAIN WASTEM (BR) HEART (HT)	1.95		. 258 × × × × × × × × × × × × × × × × × × ×	1.000 .602	MEIGHT TAKEN MEIGHT TAKEN
SPLEEN (SP)	52.		177 %	.383	WEIGHT TAKEN
KIONEY (KD)	2.79		.668 x	1.429	METGHT TAKEN
LIVER (L1)	10.21		2.412 %	5.227	
TESTIS/EPIDID (TP)	4.94		1.167 %	2.530	LEIGHT TAKEN
CLINICAL OBSERVATIONS	SNO!	+	THOLOGY OBSERUATIONS NECROPSY	υ Σ	HISTOPATHOLOGY
	CEN .	GENERAL INFORMATION (XX)	IERAL INFORMATION (XX) :	LUNG (LU) : - PERTERPHICH INFILTRATI	NG (LI): -PERIERHICHIAL/PERIUASCUI AR, INFILTRATION, LYMPHOIO,-SLIGHT

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRIA, THORACIC (AD), BIBLE, FEMIR. (FE), BOPE, STERRIM (SB), BRAIN W.STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC), DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), FYE (EY), HEART (HT), ILEIM (LL), DEJUMIM (DE), KIDNEY (KD), LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUMG (LU), MAMMARY GLAND (MG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PARTERS (FA), PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMIS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), ACOLLECTED/TAKEN (XW) THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: KIDNEY (KD), LIVER (L1)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PRITTING) LIERE SAVED ***

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/TOX SYSTEM OUTPUT *** APPENDIX 8

PRINTED: 12-MAY-83

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

450.8 GRAMS RECORDER: BARBARA DAY TERMINAL BODY MEJGHT: SACRIFICE STATUS: UNSCHEDULED (D) PATHOLOGIST: NOT REQUIRED BY PROTOCOL STUDY WEEK OF DEATH: 8 PROSECTOR: BARBARA DAY DOSE GROUP: 3 STUDY DAY OF DEATH: 51 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL DATE AND TIME OF NECROPSY: 05/31/86 14:05 DATE OF DEATH: 05/31/86 ANIMAL NUMBER: 808450

WEIGHER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

CLINICAL OBSERVATIONS

-APPEARED NORMAL

INFILTRATION, LYMPHOID, -SLIGHT -PERTERCINCHIAL APPRIVASCULAR, ILEUM (IL) SAUTOLY I C LUNG (LU): O B S E R U A T 1 O N S -MOTTLED; ALL LOBES, LIGHT TO DARK RED ALL LOBES >NOTE:>LAST IN-LIFE AND EXTERNAL GENERAL INFORMATION (XX): NECROPSY -FAILURE TO COLLAPSE; PATHULOGY (LU)

HISTOPATHOLOGY

DBSERVATIONS: NONE. FOUND DEAD AT ONE HOUR POST-DOSE OBSERVATIONS.

-FOREIGN MATERIAL, -PRESENT

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRIA, THORACIC (AD), BINNE, FEMUR (FE), BINNE, STERNIM (SB),
BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
BUDDENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), MAMMARY GLAND (MG), MAND SALIVARY GL (SG),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI),
PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SF), STOMACH, GL (ST),
STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), TRACHEA (TR), URINARY BLADDER (UB), ~COLLECTED/TAKEN (XL) THE FOLLOWING DRGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ANRTA, THORACIC (AD), BUNE, FEMUR (FE), BONE, STERNIM (SA), BRAIN W/STEM (BR), CECUM (CE), COLON (CD), CORD, CERVICAL (CS), CARD, LUMBAR (LC), CORD, THORACIC (TC), DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), JEJUNUM (JE), KIONEY (KD), LACRIMAL GI, EXB (ED) , LIVER (LI), LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL. (SG), MARRIM, STERNIM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SPLEEN (SP), STOMACH, GL. (SI), SIOMACH, NONG. (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB) FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: ፗ

*** ALL ORSANS/IISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PRITCICUL) WERE SAVED ***

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/10X SYSTEM DUTPUT *** APPENDIX B

PRINTED: 12-MAY-88 PAGE: 235

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

TERMINAL BODY WEIGHT: 449.0 GRAMS
RECORDER: SID JUNES, DUM, PHD, DACUP
WEIGHER: NOT REQUIRED BY PROTOKOL SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE PATHOLOGIST: SID JONES, DUM, PHO, DACUP STUDY WEEK OF DEATH: 14 PROSECTOR: BARBARA DAY DOSE GROUP: 3 DEATH: 96 STIJDY DAY OF POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL DATE AND TIME OF NECROPSY: 07/15/86 10:26 DATE OF DEATH: 07/15/86 ANIMAL NUMBER: 808451

*** ANIMAL HAS NO DRGAN WEIGHTS RECORDED ***

CLINICAL OBSERVATIONS

-APPEARED NORMAL

NECROPSY

COLLECTEDZTAKEN (XM) : -ELECTRON MICROSCOPY SAMPLE; LIVER >NOTE:>EXTERNAL OBSERVATIONS:NONE GENERAL INFORMATION (XX):

INFILTRATION, LYMPHOID, -SLIGHT -PERTBRONCHIAL /PERTUASCULAR 913 MINIMAL

-NEPHRIPATHY, CHRONIC PROGRESSIUE,-

KIDNEY (KD) :

HISTOPATHOLDGY

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRTA, THORACIC (AD), BONE, FEMUR (FE), BONE, STERNIM (SB),
BRAIN W/STEM (BR), CECUM (CC), CORO, CORO, CERVICAL (CS), CORO, LUMBAR (LC), CORO, THORACIC (TC),
BUDDENUM (DU), EPIDIOYMIS (EP), ESOPHAGIS (ES), EYE (EY), HEART (HT), ILEUM (IL), ABJUNIM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLANO (MS),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SU), SKIN (SK), SKIN, OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYRNID (TY), TRACHEA (TR), THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY: URINARY BLADDER (UB)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: LIVER (LI) *** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WFRE SAVED ***

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/TOX SYSTEM DUITPUT *** APPENDIX 8

PRINTED: 12-MAY-RG PAISE: 236

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

TERMINAL BODY WEIGHT: 433.6 GRAMS RECORDER: SID JONES, DUM, PHD, DACUP SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE PATHOLOGIST: SID JONES, DUM, PHD, DACUP STUDY WEEK OF DEATH: 14 PROSECTOR: BARBARA DAY DOSE GROUP: 3 STUDY DAY OF DEATH: 96 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL DATE AND TIME OF NECROPSY: 07/15/86 11:20 SEX: MALE DATE OF DEATH: 07/15/86 ANIMAL NUMBER: B08452

WEIGHER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

CLINICAL OBSERVATIONS	PATHOLOGY OBSERUATIONS NECROPSY	HISTOPATHOLOGY
-APPEARED NORMAL	KIDNEY (KD); -PELUIS, DILATED; BOTH, MEDERATELY -COLLECTED/TAKEN (XM); -ELECTRON MICROSCOPY SAMPLE; LIVER GENERAL INFORMATION (XX); -NOTE:>EXTERNAL OBSERVATIONS:NONE	KIDNEY (KD): -NEPHROPATHY, CHRONIC PROGRESSIVE,-SLIGHT -PELVIS, DILATATION,-MODERATE LUNG (LU): -PERIGRONCHIAL/PERIVASCULAR, INFILTRATION, LYMPHOID,-SLIGHT
	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRIA, THORACIC (AD), BONE, FEMUR (FE), BONE, STERNIM (SB),
BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORO, CERVICAL (CS), CORD, LIMBAR (LC), CORD, THIRACIC (TC),
DUDDENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNIM (JE), LACRIMAL GI, EXO (ED),
LIVER (LJ), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GL (SG),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERUE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PT), PITULIARY (PI),
PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SU), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), SIOMACH, BL (ST),
STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), TRACHEA (TR), URINARY BLADDER (UB) THE FOLLOWING DRGANS WERE UNREMARKABLE AT NECROPSY:

FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: LIVER (LI) 置

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STIJOY PRINTOCAL) MERE SAVED ***

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/TBX SYSTEM RUIPUT *** APPENDIX 8

PRINTED: 12-MAY-88 PAGE: 237

STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

TERMINAL BODY WEIGHT: 439.0 GRAMS
RECORDER: SID JONES, DVM, PHD, DACUP SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE STIJDY WEEK OF DEATH: 14 PROSECTOR: BARBARA DAY DOSE GROUP: 3 STUDY DAY OF DEATH: 97

WEIGHER: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHD, DACUP

*** ANIMAL HAS NO DRGAN WEIGHTS RECORDED ***

POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL DATE AND TIME OF NECROPSY: 07/16/86 8:50

DATE OF DEATH: 07/16/86 NUMBER: B08453

ANIMAL

SEX: MALE

CLINICAL DESERVATIONS

-APPEARED NORMAL

PATHOLOGY OBSERUATIONS -ELECTRON MICROSCOPY SAMPLE; LIVER GENERAL INFORMATION (XX) : NECROPSY ~COLLECTED/TAKEN (XW) :

>NOTE:>EXTERNAL DBSERVATIONS:NOME

INFILTRATION, LYMPHOLD, -SLIGHT -PERIBRINCHIAL/PERIVASCULAR -FOREIGN MATERIAL, -- PRESENT LUMB CLID :

-NEPHROPAIHY, CHRONIC PROGRESSIVE,-

KIDNEY (KD):

AIN IND

HISTOPATHOLOGY

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AD), BIRE, FEMUR (FE), BONE, STERNIM (SB),
BRAIN W/STEM (BR), CECUM (CC), CORD, CORD, CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJINUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (ED), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MS),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCRES (PA),
PARATHYROID (PT), PITULTARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL UESICLE (SU), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NOWGL (ŚU), TESTIS (ŤE), THYMUS (TH), THYROID (TY), TÂACHEA (TR), THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY: URINARY BLADDER (UB)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

*** ALL DRGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCUL) WERE SAVED ***

*** PATH/IOX SYSTEM OUTPUT *** SUBCHRONIC TOXICITY STUDY IN RATS APPENDIX 8

PRINTED: 12-MAY-BR PAGE: 238

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

TERMINAL BODY WEIGHT: 33 SACRIFICE STATUS: UNSCHEDULED (D) PATHOLOGIST: NOT REQUIRED BY PROTOCOL STUDY WEEK OF DEATH: 3 PROSECTOR: BARBARA DAY DOSE GROUP: 3 STUDY DAY OF DEATH: 19 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL DATE OF DEATH: 04/29/86 STUDY DAY OF DATE AND TIME OF NECROPSY: 04/29/86 16:17 SEX: MALE ANIMAL NUMBER: 808454

WEIGHER: NOT REQUIRED BY PROTOCOR

333.8 GRAMS

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

OBSERUATIONS NECROPSY PATHOLOGY CLINICAL OBSERVATIONS

-APPEARED NORMAL

ALL LOBES, LIGHT TO DARK RED LUNG (LU):
-FAILURE TO COLLAPSE; ALL LOBES -UNEQUALLY SIZED; LEFT, SMALL GENERAL INFORMATION (XX): > NOTE:>LAST IN-LIFE AND EXTERNAL TESTIS (TE): -MOTTLED;

INFILTRATION, LYMPHOID, -SLIGHT -PERTERCHICHIOL/PERTUASCUL AR -FORE IGN MATERIAL , - PRESENT

> UNREMARKABLE TESTIS (TE):

HISTOPATHOLOGY

OBSERVATIONS: NONE. FOUND DEAD ONE HOUR AFTER DOSING

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/TOX SYSTEM OUTPUT *** APPENDIX B

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STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

373.8 GRAMS RECORDER: BARBARA DAY TERMINAL BODY WEIGHT: SACRIFICE STATUS: UNSCHEDULFD (D) PATHOLOGIST: NOT REQUIRED BY PROTOCOL STUDY WEEK OF DEATH: 3 PROSECTOR: BARBARA DAY DOSE GROUP: 3 STUDY DAY OF DEATH: 19 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL DATE AND TIME OF NECROPSY: 04/29/86 16:17 SEX: MALE DATE OF DEATH: 04/29/86 ANIMAL NUMBER: B08454

WEIGHER: NOT REQUIRED BY PROTOCOL

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AGRIA, THORAGIC (AR), BONE, FEMIR (FE), BURIE, STERNIM (SB),
BRAIN MASTEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORAGIC (TC),
BUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNIM CIE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), MAMMARY GLAND (MG), MAND SALIVARY GL (SG),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERUE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI),
PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST),
STOMACH, NONGL (SU), THYMUS (TH), THYROID (TY), TRACHEA (TR), IRPHARY BLADDER (1B), ^COLIECTED/TAKEN (XL) THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRIA, THORACIC (AD), BURE, FEMUR (FE), BORNE, STERNIM (SB),
BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIS (TC),
BUDDENUM (DU), EPIDIOYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEMM (IL), JEJHMIM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PARICREAS (PA), PARATHYROID (PI), PITHITARY (PI),
PROSTATE (PR), RECTUM (RE), SEMINAL UESICLE (SU), SKIN (SK), SPLEEN (SP), STOMACH, GL (SI), STOMACH, NUNGL (SU),
THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (LB) THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WFRE SAVED ***

APPENDIX 8 *** PATH/TOX SYSTEM DUTPUT *** SUBCHRONIC TOXICITY STIDDY IN RAIS

PRINTED: 12-MAY-88 PAGE: 240

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

	SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE	TERMINAL FIRDY METCHT: 463.3 SEAMS	RECORDER: SID JONES, DUM, PHD, DACUP	WEIGHER: NOT REGULRED BY PROTOCOL	
	TUS:		BARA DAY	PATHOLOGIST: SID JONES, DUM, PHD, DACUP	
•	DOSE GROUP: 3	· DEAT	PROSECTOR: BARBARA DAY		
	SEX: MALE	STUDY DAY O	: 07/16/86 10:33	UIRED BY PROTOCO	
	ANIMAL NUMBER: 808455	DATE OF DEATH: 07/16/86	DATE AND TIME OF NECROPSY: 07/16/86 10:33	POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL	

*** ANIMAL HAS NO DRGAN WEIGHTS RECORDED ***

	PATHOLOGY OBSERVATIONS	
CLINICAL DBSERUATIONS	NECROPSY	HISTOPATHOLOGY
-BOTH EYES-CHROMODACRYORRHEA	^COLLECTED/TAKEN (XW) :	CONS (LU) :
	-ELECTRON MICROSCOPY SAMPLE; LIUFR	-PERIBROHICHIAL /PERIUASCULAR,
	GENERAL INFORMATION (XX) :	INFILTRATION, LYMPHOID, -SILGHT
	ANDTE: VEXTERNAL DRSERUATIONS: ROTH EYES-	
	CHROMODACRYORRHEA	
		i

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRTA, THORACIC (AD), BONE, FEMUR (FF), BONE, STERNUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CORO, LUMBAR (LC), CORD, THORACIC (TC),
BUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (LL), JEJUNIM (SF), KICHEY (KD),
LACRIMAL GL, EXD. (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MISCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PARCREAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TF), THYMIS (TH), THYROID (TY), TRACHFA (TR), THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: KIDNEY (KD), LIVER (LI)

*** ALL ORGANSZIJSSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTRICAL) WERE SAUED ***

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/TOX SYSTEM DITTPUT *** APPENDIX 8

PRINTED: 12-MAY-8S PAGE: 241

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY MUMBER: 2399108

TERMINAL BODY WEIGHT: 495.9 GRAMS RECARDER: SID JONES, DUM, PHD, DACUP WETGHER: NOT REQUIRED BY PROTOCOL SACRIFICE STATUS: SCHEDULFD, TERMINAL SACRIFICE PATHOLOGIST: SID JONES, DUM, PHD, DACUP STUDY WEEK OF DEATH: 14 PROSECTOR: DOUGLAS HERNDON DOSE GROUP: 3 STUDY DAY OF DEATH: 97 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL AND TIME OF NECROPSY: 07/16/86 11:28 DATE OF DEATH: 07/16/86 ANIMAL NUMBER: 808456

*** ANIMAL HAS NO DRGAN WEIGHTS RECORDED ***

CLINICAL DBSERVATIONS

-APPEARED NORMAL

PATHOLOGY OBSERUATIONS NECROPSY

*COLLECTED/IAKEN (XW) :
-ELECTRUN MICROSCOPY SAMPLE; LIUER

INFILTRATION, LYMPHOID, -SLIGHT - PERTRRUNCHIAL ZPERTUASCULAR CONG (LU)

HISTOPATHOLOGY

>NOTE:>EXTERNAL OBSERVATIONS:NOVE GENERAL INFORMATION (XX) :

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AN), BONE, FEMUR (FE), BONE, STERNUM (SB), BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORO, CRVICAL (CS), CORD, LUMBAR (LC), CORO, THORACIC (TC), DUDODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HI), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LI), MARMMARY SLAND (MS), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PARCHERS (PA), PARCHERS (PA), SPATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SFMINAL VESICLE (SU), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, GL (ST), TEACHER (TR), THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: KIDNEY (KD), LIVER (LI) 표

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PRITOCOL) WERE SAVED ***

APPENDIX 8 *** PATH/TOX SYSTEM CHITPLIT *** SUBCHRONIC TOXICITY STUDY IN RATS

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STUDY NIMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: 808457 SEX: MALE DATE OF DEATH: 07/15/86 STUDY DAY OF DATE AND TIME OF NECROPSY: 07/15/86 8:09 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL	- ОЕАТН	WEEK C ARA DAY D JONES	SCHE Term	SCHFDULED, TERMINAL SACRIFICE TERMINAL BODY WEIGHT: 530.9 GRAMS RECORDER: SID JONES, DUM, PHD, DACUP WEIGHER: BARBARA DAY
ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO	ORGAN STATUS
ADRENAL (AD)	0.90	. 0113 %	. 11289	MEIGHT TAKEN
BRAIN MYSTEM (BR)	2.07	389 %	1.000	METCHT TAKEN
HEART (HT)	1.17	.220 %	.565	LEISHT TOKEN
SPI FFN (SP)	29.	.119 %	.306	WEIGHT TAKEN
KIDNEY (KD)	3.48	.456 %	1.685	METGHT TAKEN
LIUER (LI)	12.24	2.306 %	5.925	WEIGHT TAKEN
TESTIS/EPIDID (TP)	5.04	. 948 %	2.437	WEIGHT TAKEN
CLINICAL OBSERVATIONS	PATHOL	THOLOGY OBSERUATIONS NECROPSY	S N O	HISTOPATHOLOGY
-APPEARED NORMAL	GENERAL INF	GENERAL INFORMATION (XX): > NOTE:> EXTERNAL OBSERUATIONS: NONE	KIDNEY (KD) -NEPHETPATH SLIGHT -GRANN AR CI LUNG (LU): -PERIBEDNCH	KIDNEY (KD): -NEPHRIPATHY, CHRONIC PROGRESSIVE,- SLIGHT -GRANIW AR CASTS,-SLIGHT -LUNG (LU): -NET IRRAICHAL/PERIVASCIMAR,

APPENDIX 8 *** PATH/IOX SYSTEM OUITPLIT *** SUBCHRONIC TOXICITY STLIDY IN RATS

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INDIVIDUAL ANIMAL SUMMARY REPURT

STUDY NUMBER: 2399108

TERMINAL BODY WEIGHT: 530.9 GRAMS RECORDER: SID JONES, DUM, PHD, DACUP SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE WE I GHER: BARBARA DAY PATHOLOGIST: SID JONES, DUM, PHO, DACUP STUDY WEEK OF DEATH: 14 PROSECTOR: BARBARA DAY DOSE GROUP: 3 DATE OF DEATH: 07/15/86 STUDY DAY OF DEATH: 96
DATE AND TIME OF NECROPSY: 07/15/86 8:09 PRUSE POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL ANIMAL NUMBER: 808457

ADRENAL, CORTEX (ACT), ADRENAL, MEDULLA (CM), AGRIA, THORACIC (AD), BOBLE, FEMUR (FE), BOBLE, SIERHEM (SB),
BRAIN WASTEM (BR), CECUM (CC), CORO, CORD, CERUICAL (CS), CORO, LUMBAR (LC), CORO, THORACIC (TC),
BRODDENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEIM (IL), JEJUHEM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MS),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERUE, SCIATIC (SN), PAPICRE'AS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SU), SKIN (SK), SKIN, OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR),
URINARY BLADDER (UB), ACOLLECTED/TAKEN (XW) THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: LIVER (LI) *** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STIDY PROTOCOL) WERE SAVED ***

*** PATH/TÜX SYSTEM DUTPIJT *** APPENDIX 8

SUBCHRONIC TOXICITY STUDY IN RATS

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INDIVIDUAL ANIMAL SUMMARY REPORT

STHOY NUMBER: 2399108

216.1 GRAMS RECORDER: KIM LINCOLN TERMINAL BODY WEIGHT: SACRIFICE STATUS: UNSCHEDULED (D) PROSECTOR: KIM LINCOLN PATHOLOGIST: NOT REMJIRED BY PROTOCOL STUDY WEEK OF DEATH: 1 DOSE GROUP: 3 ANIMAL NUMBER: B08458 SEX: MALE
DATE OF DEATH: 04/14/86 STUDY DAY OF DEATH: 4
DATE AND TIME OF NECROPSY: 04/14/86 12:30 PROS
POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL PATH

WEIGHER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

	PATHOLOGY OBSERVATIONS	
CLINICAL OBSERVATIONS	NECROPSY	HISTOPATHO
-APPEARED NORMAL	CUNG (LU) :	ADRENAL, CORTEX (AC) :
	-FAILURE TO COLLAPSE; ALL LORES	-INTI ATERALLY EXAMINED
	-MOTTLED; ALL LOBES, WHITE TO RED	ADRENAL, MEDULLA (AM) :
	GENERAL INFORMATION (XX):	-UNIT ATERALLY EXAMINED
	SNOTE: SLAST IN-LIFE AND EXTERNAL	CECUM (CE) :
	CIBSERVATIONS: NONE	S AUTOL YTIC

D,-PRESENT D,-PRESENT INFILTRATION, LYMPHOID, -SLIGHT -PERIBRONCHIAL/PERIUMSCULAR, 10 DGY DUCIDENLIM (DID : SERINALM (JE) : 11.EUM (11.) : **AUTOLYTIC** > PHITOLYTIC SALITOLYTIC > AUTOLYTIC >ALITOLYTIC LUMB CLUD : EYE (EY) :

PARATHYRNID (PT): SECTION EXAMINED; TISSUE NOT PRESENT

RECTUM (RE):

> AUTOLYTIC **MANTOLYTIC**

STOMACH, GL

HRIMARY RIADDER (UR)

> AUTOLYTIC

-FOREIGN MATERIAL, -PRESENT

-CONSESTION, -MODERATE

APPENDIX 8 *** PAIH/IOX SYSTEM DUTPUI *** SLIBCHRONIC TOXICITY STUDY IN RAIS

PRINTED: 12-MAY-811 PAGE: 245

STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

WEIGHER: NOT REQUIRED BY PROTOCOL RECORDER: KIM LINCOLN TERMINAL BOOY WEIGHT: SACRIFICE STATUS: UNSCHEDULED (D) PATHOLOGIST: NOT REQUIRED BY PROTOCOL STUDY WEEK OF DEATH: 1 PROSECTOR: KIM LINCOLN DOSE GROUP: 3 DATE OF DEATH: 04/14/86 STUDY DAY OF DEATH: 4 DATE AND TIME OF NECROPSY: 04/14/86 12:30 PROS POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL SEX: MALE ANIMAL NUMBER: B08458

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERMUM (SB),

BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),

BUDDENUM (DU), EPIDIOYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEIM (IL), JEJUMUM (JE), KIDHEY GI (SB),

LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), MAMMARY GLAND (MG), MAND SALIVARY GI (SB),

MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PT), PITILITARY (PI),

PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST),

STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (18), ACOLLECTED/TAKEN (XW)

AORTA, THORACIC (AO), BONE, FEMUR (FE), BUNE, STERNUM (SB), BRAIN W/STEM (RR), CORD, CERUICAL (CS),
CORD, LUMBAR (LC), CORD, THORACIC (TC), EPIDIDYMIS (EP), ESOPHAGUS (ES), HEART (HT), KIDNEY (KD), LACRIMAL GL, EXO (ED)
, LIVER (LI), LN, MESENTERIC.(MS), MAMMARY GLAND (MG), MAND SALIVARY (R), MARROW, STFRNUM (SE),
MUSCLE, SKELETAL (SM), NERUE, SCIATIC (SN), PANCREAS (PA), PITUITARY (PI), PROSTATE (PR), SEMINAL UESICLE (SV),
SKIN (SK), SPLEEN (SP), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHFA (TR) THE FOLLOWING TISSIJES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

APPENDIX 8 *** PATH/TOX SYSTEM QUIPUT *** SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88 PAGE: 246

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

TERMINAL RODY WEIGHT: 495.7 GRAMS
RECORDER: SID JONES, DVM, PHD, DACUP
WEIGHER: NOT REGAIRED BY PROTOCOL SACRIFICE STATUS: SCHEDILLED, TERMINAL SACRIFICE PATHOLOGIST: SID JONES, DUM, PHD, DACUP STUDY MEEK OF DEATH: 14 PROSECTOR: BARBARA DAY DOSE GROUP: 3 DEATH: 97 STUDY DAY OF POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL DATE AND TIME OF NECROPSY: 07/16/86 11:57 DATE OF DEATH: 07/16/86 ANIMAL NUMBER: B08459

*** ANIMAL HAS NO DRGAN WEIGHTS RECORDED ***

CLINICAL OBSERVATIONS	PATHOLOGY OBSERUATIONS NECROPSY	HISTOPATHOLOGY
* * * * 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1		
APPEARED NORMAL	^COLLECTED/TAKEN (XW) :	LUNG (LU) :
	-ELECTRON MICROSCOPY SAMPLE; LIVER	-PERTERBUCHIA ZPERTUASCHLAR,
	GENERAL INFORMATION (XX) :	INFILTRATION, LYMPHOID, - SLIGHT
	>NOTE:>EXTERNAL DBSERVATIONS:NONE	
		1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
THE ROLL OF INTERPOLATION OF THE PARTY OF TH	AT 10000000.	

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRIA, THORACIC (AD), BINE, FEMIUR (FE), BONE, STERNUM (SB), BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORO, CERVICAL (CS), CARD, LUMBAR (LC), CARD, THORACIC (TC), DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEARI (HI), ILEUM (IL), DEJUNUM (3E), KIDNEY (KD), LACRIMAL GL, EXO (EO), LIVER (LI), LAMBAR (LI), MANDERY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PI), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEM)MAL UFSICLE (SU), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHER (TR), FULLUWING URGANS WERE UNREMARKABLE AT NECROPSY: JRINARY BLADDER (UB) ¥

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: KIDNEY (KD), LIVER (LI)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STIMY PROTOCOL) WERE SAVED ***

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/10X SYSTEM DUTPUT *** APPENDIX 8

PRINTED: 12-MAY-86 PAISE: 247

STUDY NUMBER: 2399188

INDIVIDUAL ANIMAL SUMMARY REPURT

: 888460 : 07/16/86 OF NECROPSY: 07/ HER: NOT REQUIRED	. ОЕАТН	WEEK LAS HE D JONE		SCHFDLLED, TERMINAL SACRIFICE TERMINAL BODY WEIGHT: 495.7 GRAMS RECORDER: SID JONES, DUM, PHD, DACUP WEIGHER: DOUGLAS HERNOON
ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN MEIGHT RATIO	ORGAN STATUS
!	. 063	. 0127 %	7620.	METCHT TAKEN
HEART (HT)	2:12 1:30	262.	.612	
SPLEEN (SP)	.94	.189 %	. 443	
KIDMEY (KD)	3.17	.640 %	1.497	
	13.43	2.710 %	6.338	
TESTIS/EPIDIO (TP)	5.39	1.086 %	2.541	METCHT TAKEN
CLINICAL OBSERVATIONS	Œ Œ	THOLOGY OBSERUATIONS NECROPSY	SZO	HISTOPATHOLOGY
- APPEARED NORMAL.	GENERAL INFO	GENERAL INFORMATION (XX); >NOTE;>EXTERNAL OBSERVATIONS:NOME	KIDNEY (KD) : -NEPHREFAIHY MINIMAL LIVER (LI) : -FOCI OF MOR	DNEY (KD); -NEPHREFAIHY, CHRONIC FROGRESSIVE,- MINIMAL VER (LI); -FOCI OF MONONICLEAR CELLS,-MINIMAL

INFILTRATION, LYMPHOID, -SLIGHT

-PERIBRONCHIAL/PERIUASCULAR

LING (LU) :

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRTA, THORACIC (AD), BOHE, FEMUR (TE), BOHE, STERRUM (SB),

BRAIN WASTEM (BR), CECUM (CE), COLON (CD), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),

BRAIN WASTEM (BR), CECUM (CE), COLON (CD), CORD, CERVICAL (CS), LIVER (LC), JEJURUM (JE), KIDNEY (KD),

LACRIMAL GL, EXO (ED), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MS),

MAND SALIVARY GL (SG), MARROW, STERNIM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PARITREAS (PA),

PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SU), SKIN (SK), SKIN, DTHER (SS),

SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMIS (TH), THYROID (TY), TRACKLA (TR),

URINARY BLADDER (UB), ACOLLECTED/TAKEN (XW)

^{***} ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

A** PATH/TOX SYSTEM OUTPUT ***

SUBCHRONIC TOXICITY STUDY IN RATS

INDIVIDUAL ANIMAL SUMMARY REPORT

PRINTED: 12-MAY-8A PAGE: 248

STHDY NUMBER: 2399108

TERMINAL BODY WEIGHT: 503.6 GRAMS RECIRDER: SID JONES, DUM, PHD, DACUP SACRIFICE STATUS: SCHFDULED, TERMINAL SACRIFICE STUDY WEEK OF DEATH: 14 PROSECTOR: TIM GROUE DOSE GROUP: 3 DATE OF DEATH: 07/16/96 STUDY DAY OF DEATH: 97
DATE AND TIME OF NECROPSY: 07/16/96 11:49 PROSE ANIMAL NUMBER: B08461

POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL		PATHOLOGIST: SID JONES, DUM, PHD, DACUP	DACUP MEIGHER: TIM GRIDUE	im groue
TARY NOTED	ABSOLUTE ORGAN WEIGHT	ORGAN WEIGHT RELATIVE	ORGAN TO BRAIN	ORGAN STATUS
			1 1 1 1 1	!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!
ADREMAL (AD)	.072	.0143 %	. 0365	MEIGHT TAKEN
BRAIN W/STEM (BR)	1.97	391 %	1.000	WEIGHT TAKEN
	1.39	₹ 575.	.706	WEIGHT TAKEN
SPLEEN (SP)	.81	.161 %	.411	WEIGHT TAKEN
KIDNEY (KD)	3.54	% €0Z.	1.797	WEIGHT TAKEN
LIVER (LI)	14.56	2.891 %	7.391	WEIGHT TAKEN
TESTIS/EPIDID (TP)	5.02	% Z66°	2.548	WEIGHT TAKEN
	P A T H O L O G	ATHOLOGY OBSERVATIONS	S N O	
CLINICAL OBSERVATIONS		NECROPSY		HISTOPATHOLOGY
-APPEARED NORMAL.	GENERAL INFORMATI	GENERAL INFORMATION (XX) : >NOTE:>EXTERNAL OBSERVATIONS:NONE	KIONEY (KD): -PYEL DREPHRI	ONEY (KD): -PYELONEPHRITIS,-SLIGHT

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRIA, THORACIC (AL), BONE, FEMUR (FE), BINTE, STERNIM (CB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CORD, LUMBAR (LC), CORO, THORACIC (TC),
BRAIN W/STEM (BR), CECUM (CE), ESOPHAGIS (ES), EYE (EY), HEART (HT), ILEUM (LL), JEJUNIM (JF), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MS),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NEPUE, SCIATIC (SN), PANCREAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV); SKIN (SK), SKIN, OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONSL (SU), TESTIS (TE), THYMIS (TH), THYROID (TY), TRACHEA (TR), THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

INFILTRATION, LYMPHOID, -MINIMAL

-PERIBRONCHIAL /PERIUASCULAR

FUNG (LL):

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: LIVER (LI) *** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY FROTOCOL) WERE SAUFD ***

A** PATH/TOX SYSTEM CLITPUT *** SUBCHRONIC TOXICITY STUDY IN RAIS

PRINTED: 12-MAY-88 PAGE: 249

STUDY NUMBER: 2399188

INDIVIDUAL ANIMAL SUMMARY REPORT

POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL	PRUIGLUE PHINGLESISIS SID JONES, DVII, THUS, DRIVE			
DRGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	DRSAN TO BRAIN WEIGHT RATIO	STATUS
ADREMAL (AD) BRAIN W/STEM (BR)	. 047	. 0101 %	.0219	WEIGHT TAKEN WEIGHT TAKEN
HEART (HT) SPLEEN (SP)	1.24	.163 %	178. 1888.	
KIDNEY (KD) LIUER (LI) TESTIS/EPIDID (TP)	3.52 13.30 4.95	2.852 % 1.062 %	1.65% 6.186 2.382	1
CLINICAL OBSERVATIONS	T & G	HOLOGY OBSERUATIONS NECROPSY	S N	HISTOPATHOLOGY
- APPEARED NORMAL	LUNG (LU) : LUNG (LU) : -DARK AREA POSTERIOR GENERAL INFO	LUNG (LU): -DARK AREA; LEFT APICAL LOBE, POSTERIOR AREA, DARK RED, 1.0 × 1.0 CM GENERAL INFORMATION (XX): >NOTE:>EXTERNAL ORSERVATIONS: HONE	17 17 1	NE, FEMUR (FE): -ARTICULAR SURFACE HUT PRESENT,-PRESENT UER (L.I): -(MULTI)FOCAL NECROSTS,-MODERATE NG (L.U): -PERIBRONCHIAL/PERTUASCULAR; INFILTRATION, LYMPHOLD,-SLISHI

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/TOX SYSTEM DUTPLIT *** APPENDIX B

PRINTED: 12-MAY-88

SUMMARY REPORT INDIVIDUAL ANIMAL

STUDY NUMBER: 2399108

TERMINAL BODY WEIGHT: 466.3 GRAMS RECORDER: SID JONES, DUM, PHD, DACUP SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE WEIGHER: BARBARA DAY PATHOLOGIST: SID JONES, DUM, PHD, DACUP STUDY WEEK OF DEATH: 14 PROSECTOR: BARBARA DAY DOSE GROUP: 4 DATE OF DEATH: 07/14/86 STUDY DAY OF DEATH: 95
DATE AND TIME OF NECROPSY: 07/14/86 8:56 PRINSE POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL SEX: MALE ANIMAL NUMBER: B08482 DATE OF DEATH: 07/14/86

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AD), BONE, FEMIR (FE), BONE, STERNUM (SB),
BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORO, CERUICAL (CS), CORO, LUMBAR (LC), CORO, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HI), ILEIM (IL), JEJINUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), MAMMARY GLAND (MS), MAND SALIVARY GL (SG),
MASCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (FI), PITUITARY (PI),
PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST),
STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (18), ACCULECTED/TAKEN (XW)

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRIA, THORACIC (AN), BONE, STERNUM (SA), BRAIN W/SIEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORO, THORACIC (TC), DUNDENUM (DI), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LAFRIMAL GI, EXO (FO), LANDMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MISCLE, SKELETAL (SM), NERUE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PT), PITHITARY (PI), PROSTATE (PR), RECTUM (RE), SFMIHAI UESICLE (SU) SKIN (SK), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB) FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: Ŧ

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STIMY PROTONI) WERE SAVED ***

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/TOX SYSTEM OUTPUT *** APPENDIX 8

PRINTED: 12-MAY-88

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

TERMINAL BODY WEIGHT: 452.5 GRAMS RECORDER: SID JONES, DVM, PHD, DAILUP SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE PATHOLOGIST: SID JONES, DUM, PHD, DACUP 1: 95 STIDY WEEK OF DEATH: 14 PROSECTOR: DOUGLAS HERNDON DOSE GROUP: 4 DEATH: 95 STUDY DAY OF POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL DATE AND TIME OF NECROPSY: 07/14/86 9:40 SEX: MALE DATE OF DEATH: 07/14/86 ANIMAL NUMBER: B08483

WETGHER: NOT REQUIRED BY PROTORON

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

CLINICAL OBSERVATIONS

-RIGHT EYE-CHROMODACRYORRHEA

NECROPSY

OBSERUATIONS

PATHOLOGY

-ELECTRON MICROSCOPY SAMPLE; LIVER GENERAL INFORMATION (XX): ^COLLECTED/TAKEN (XW) :

NOTE:>EXTERNAL OBSERVATIONS:RIGHT EYE-CHROMODACRYORRHEA

-NEPHROPATHY, CHRONIC PROGRESSIVE,-HISTOPATHOLOGY KIDNEY (KD) :

-FOCI OF MONUNCLEAR CELLS, -MINIMAL LIVER (LI) : 111111

MINIMAL

>SECTION EXAMINED, TISSUE NOT PRESENT THETETRATION, LYMPHOID, - SEIGHT -PERIBRONCHIAL/PERIVASCULAR, PARATHYROID (PT) :

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/TOX SYSTEM DUTPUT *** APPENDIX 8

PRINTED: 12-MAY-88

STUDY NUMBER: 2399108

INDIVIDIJAL ANIMAL SLIMMARY REPURT

DOSE GROUP: 4

SEX: MALE

ANIMAL NUMBER: B08483

11NAL BODY WEIGHT: 452.5 GRAMS RECORDER: SID JONES, DUM, PHD, DACUP WEIGHER: NOT REQUIRED BY PROTOCOL SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE TERMINAL BODY WEIGHT: STUDY WEEK OF DEATH: 14 PROSECTOR: DOUGLAS HERNDON

PATHOLOGIST: SID JONES, DUM, PHD, DACUP THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY: DATE OF DEATH: 07/14/86 STUDY DAY OF DEATH: 95
DATE AND TIME OF NECROPSY: 07/14/86 9:40 PROSE POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRTA, THURACIC (AD), BIDNE, FEMIR (FE), BIDNE, STERNIM (SB),
BRAIN W/SIEM (BR), CECUM (CE), COLON (CO), CORD, CERUICAL (CS), CORD, LUMBAR (LC), CORD, THURACIC (TC),
DUDÓBNUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEMM (IL), AFJINNIM (JF), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MIS),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PARTREAS (FA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NOWGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB)

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRTA, THORACIC (AD), BIDNE, FEMUR (FE), BIDNE, STERNIM (SB),
BRAIN WASTEM (BR), CECUM (CE), COLON (CD), COND, CFRUICAL (CS), CHRD, LIMBAR (LC), CORD, THORACIC (TC),
BUDDENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), LACRIMAL GL, EXD (ED),
LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARRIM, STERNIM (SE), MUSCI E, SKELETAL (SM),
NERUE, SCIATIC (SN), PANCREAS (PA), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL UESICLE (SU), SKIN (SK),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYRIUD (TY), TRACHEA (TR), FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: URINARY BLADDER (UB) ͳ

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WARE SAVED ***

SURCHRONIC TOXICITY STUDY IN RATS *** PATH/TOX SYSTEM DUTPIJT *** APPENDIX 8

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INDIVIDIAL ANIMAL SIJMMARY REPORT

STUDY NUMBER: 2399108

SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE
DF DEATH: 14 TERMINAL BODY WEIGHT: 651.8 GRAMS
Y
RECORDER: SID JONES, DUM, PHD, DACUP PATHOLOGIST: SID JONES, DUM, PHD, DACUP STUDY WEEK OF DEATH: 14 PROSECTOR: BARBARA DAY DOSE GROUP: 4 STUDY DAY OF DEATH: 95 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL DATE AND TIME OF NECROPSY: 07/14/86 11:12 SEX: MALE DATE OF DEATH: 07/14/86 ANIMAL NUMBER: B08484

WETGHER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO DRGAN WEIGHTS RECORDED ***

HISTOPATHOLOGY BONE, FEMUR PATHOLOGY OBSERUATIONS NECROPSY *COLLECTED/TAKEN (XW) : CLINICAL OBSERVATIONS -APPEARED NORMAL

-ELECTRON MICROSCOPY SAMPLE; LIVER >NOTE:>EXTERNAL DBSERUATIONS:NONE GENERAL INFORMATION (XX) :

-ARTICULAR SURFACE NOT PRESENT, - PRESFNT -NEPHROPAIHY, CHRONIC PROGRESSIVE,-- (MULTI) FOCAL NECROSIS, - SLIGHT - PERTERDINCHTAL / PFRTUASION AR (FE) -KIDNEY (KD): CL10 : CLING (CLB) : MINIMAL LIUER

INFILTRATION, LYMPHOID, -SLIGHT

*** PATH/10X SYSTEM OUTPUT *** SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88 PAGE: 254

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY MIMBER: 2399108

SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE	TERMINAL BODY WEIGHT: 651.8 GRAMS	RECORDER: SID JONES, DUM, PHD, DACUP	WEIGHER: NOT REGISTRED BY PROTOCOL	***************************************
	STUDY WEEK OF DEATH: 14	ARBARA DAY	PATHOLOGIST: SID JONES, DUM, PHD, DACUP	102211111111111111111111111111111111111
DOSE GROUP: 4	STUDY DAY OF DEATH: 95 STU	PROSECTOR: BARBARA DAY		
SEX: MALE		5Y: 07/14/86 11:12	EQUIRED BY PROTOCOL	
ANIMAL NUMBER: 808484	DATE OF DEATH: 07/14/86	DATE AND TIME OF NECROPSY: 07/14/86 11:12	POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL	

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRIA, THORAGIC (AD), BONE, FEMIR (FE), BONE, STERNIM (SB),
BRAIN WASTEM (BR), CECUM (CC), CORO, CORO, CORO, LUMBAR (LC), CORO, THORACIC (TC),
BUNDENUM (DU), EPIDIOYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (1L), DEDUNUM (3E), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GI AND (MS),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), FAWIREAS (FA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RF), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NUMBL (SU), TESTIS (TE), THYRUS (TH), THYROID (TY), TRACHEA (TR), THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY: URINARY BLADDER (UB) FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRIA, THORACIC (AD), BONE, STERNUM (SB), BRAIN W.STEM (BR), CECUM (CE),
COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC), DIODENUM (DI), EPIDIDYMIS (EP),
ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNIUM (JE), LACRIMAL AL, EXD (ED), LN, MESENTERIC (MS),
MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MISCLE, SKELETAL (SM), NERUE, SCIATIC (SN),
PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SFMINAL VESICLE (SU), SKIN (SK),
SPLEEN (SP), STOMACH, GL (SI), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR), JRINARY BLADDER (UB) 뿔

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STIMY PROTINCIL) WERE SAVED ***

*** PATH/TOX SYSTEM OUTPUT *** SUBCHRONIC TOXICITY STUDY IN RATS

PRINTFD: 12-MAY-8E PAGE: 255

STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: 808485 SEX: MALE DATE OF DEATH: 07/14/86 STUDY DAY OF DATE AND TIME OF NECROPSY: 07/14/86 13:07 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL	DEATH	WEEK D	SCHE	DULED, TERMINAL SACRIFICE INAL BODY WEIGHT: 359.5 GRAMS RECCROPER: SID JONES, DUM, PHD, DACUP WEIGHER: IIM GROUE
ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	DRGAN TO BRAIN MEJGHT RATIO	ORGAN STATUS
ADREMAL (AD) BRAIN W/STEM (BR) HEART (HT) SPLEEN (SP) KIDNEY (KD) LIVER (LI) TESTIS/EPIDIO (TP)		. 0147 % . 531 % . 304 % . 174 % . 838 % 3.009 %	. 0277 1.000 . 5.71 . 327 1.578 5.663	METGHT TRKEN
CLINICAL OBSERVATIONS	T & 9	HOLOGY OBSERUATION NECROPSY	BNS	нізторатнопову
-APPEARED NORMAL	GENERAL INFO	GENERAL INFORMATION (XX): >MOTE:>EXTERMAL OBSERVATIONS:NONE	KIDNEY (KD): -NEPHKOPATHY, CHRON-SLIGHT -LIAG (LB): -PERIBRONCHIAL/PERINFILITRATION, LYMPHAMMARY GLAND (MG):	DNEY (KD): -NEPHKOPATHY, CHRONIC PROGRESSIVE,- SLIGHT NG (LI): -PERIBRONCHIAL/PERIUASCHLAR, INFILTRATION, LYMPHOID,-SLIGHT AMMARY SLAND (MG): >SECTION EXAMINED; TISSIE NOT PRESENT

APPENDIX 8 *** PAIH/IDX SYSTEM QUIPUI *** SUBCHRONIC IQXICITY STUDY IN RAIS

PRINTFO: 12-MAY-RS PACE: 254

STLIPY NUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

RECORDER: SID JONES, DUM, PHD, DACUP 359.5 GRAMS SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE TERMINAL BODY WEIGHT: WEIGHER: TIM GROUE PATHOLOGIST: SID JONES, DUM, PHD, DACUP STUDY WEEK OF DEATH: 14 . PROSECTOR: TIM GROUE DOSE GROUP: 4 DEATH: 95 STUDY DAY OF POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL AND TIME OF NECROPSY: 07/14/86 13:07 SEX: NO. F DATE OF DEATH: 07/14/86 ANIMAL NUMBER: B08485

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRIA, THORACIC (AD), EDRE, FEMUR (FE), BOHE, SIFRNUM (SB),
BRAIN WISTEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORO, THORACIC (TC),
BUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGIS (ES), EYE (EY), HEART (HT), ILEUM (IL), ABUINAM (JE), KIONEY (KD),
LACRIMAL GL, EXO (ED), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MS),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANGREAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMIS (TH), THYROID (TY), TRACHEA (TR),
URINARY BLADDER (UB), ACOLLECTED/TAKEN (XW) THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AONTA, THORACIC (AO), BONE, FEMUR (FE), BONE, STERNIM (SB),

BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORD, CFRUICAL (CS), CORD, FUMBAR (LC), CORD, THORACIC (TC),

DUDDENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (DF), LACRIMAL (G),

LIVER (LI), LN, MESENTERIC (MS), MAND SALIVARY GL (SG), MARROW, SIERMIM (SE), MUSCIE, SKELETAL (SM),

NERUE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RF), SEMINAL UESICLE (SU),

SKIN (SK), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONSL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY),

TRACHEA (TR), URINARY BLADDER (UB) 뿔

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAUED ***

APPENDIX 8 *** PATH/TOX SYSTEM DUITPUT *** SUBCHRONIC TOXICITY STLOY IN RATS

PRINTED: 12-MAY-88 PAGE: 252

STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL SHMMARY REPORT

		1		
ANIMAL NUMBER: 808486 SEX; MALE DATE OF DEATH: 07/14/86 STUDY DAY OF DEATH: DATE AND TIME OF NECROPSY: 07/14/86 13:33 PR POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL PA	SEX; MALE 00SE GROUP: 4 STUDY DAY OF DEATH: 95 STUDY 14/86 13:33 PROSECTOR: TIM 9 BY PROTOCOL PATHOLOGIST: SII	LEEK C SROVE D JONES	SCHE TERM	SCHEDULED, TERMINAL SALKIFITE TERMINAL BODY WEIGHT: 444.2 GRAMS RECORDER: SID JONES, DUM, PHD, DACUP WEIGHER: TIM GROUE
	ABSOLUTE ORGAN WEIGHT	ORGAN WEIGHT RELATIVE	ORGAN TO BRAIN	S A B A B A B A B A B A B A B A B A B A
ORGAN NAME	(GRAMS)	TO MILE METERN (%)		
ADRENAL (AD)	. 053	, 0119 x	.0263	METGHT TAKEN
BRAIN W/STEM (BR)	2.00	. 451 %	1.000	
	1.13	254 K	. 563	_
SPLEEN (SP)	.54	.120 %	.267	_
KIDNEY (KD)	3,15	710 %	1.574	-
I IUER (LI)	13.27	2.987 %	6.623	•
TESTIS/EPIDIO (TP)	5.57	1.253 %	2.779	METCHT TAKEN
CLINICAL DBSERUATIONS	PATHOL	HOLOGY OBSERUATI NECROPSY	s z	HISTOPATHOLOGY
-APPEARED NORMAL	GENERAL INFO	GENERAL INFORMATION (XX): >HOTE:>EXTERNAL ORSERVATIONS:HONE	EYE (EY): -CHEONIC IN SLIGHT LING (L!!): -PERIBRONCH INFILTRATI	E (EY): -CHEONIC INFLAMMATION, MARDFRIAN GLAW),-SLIGHT NG (L!!): -PERIBRONCHIAL/PERIDAGCULAR, INFILTRATION, LYMPHOLD,-SLIGHT

APPENDIX 8 *** PATH/IOX SYSTEM CLITPLIT *** SUBCHRONIC TOXICITY STLIDY IN RATS

PRINTED: 12-MAY-89 PAGE: 258

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

TERMINAL BODY WEIGHT: 444.2 GRAMS RECRIRDER: SID JONFS, DUM, PHD, DAEUP SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE WEIGHER: TIM GROUE PATHOLOGIST: SID JONES, DUM, PHD, DACUP STIJDY WEEK OF DEATH: 14 PROSECTOR: TIM GROVE DOSE GROUP: 4 DEATH: 95 DATE OF DEATH: 07/14/86 STLIDY DAY OF DATE AND TIME OF NECROPSY: 07/14/86 13:33 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL SEX: MALE ANIMAL NUMBER: 808486

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRIA, THORACIC (AD), BONE, FEMIR (FE), BONE, STERNUM (SB),
BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORO, CERVICAL (CS), CORO, LUMBAR (LC), CORO, THORACIC (TC),
BLODDENUM (DU), EPIDIOYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNIM (JE), KIONEY (KO),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GI AND (MG),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERUE, SCIATIC (SN), PANTOREAS (PA),
PARATHYROIO (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONSL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR),
URINARY BLADDER (UB), ~COLLECTED/TAKEN (XW) THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

FOLLOWING TISSUES WERE LINREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRIA, THORACIC (AO), BONE, FEMIJR (FE), BONE, STERNUM (SB),

BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),

DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXO (FO),

LIUER (LI), LN, MESENTERIC (MS), MAMMARY GLAND (MS), MAND SALIVARY GL (SR), MARREIM, STERMUM (SE),

MUSCLE, SKELETAL (SM), NERUE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR),

RECTUM (RE), SEMINAL UESICLE (SU), SKIN (SK), SPLEEN (SP), STOMACH, GL (ST), STOMACH, MIRTAL (SID), IFSTIS (TE),

THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB) Ή

*** ALL ORGANS/TISSUES (REGUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/TOX SYSTEM QUIPUT *** APPFINDIX B

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INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NIMBER: 2399108

SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE TERMINAL BROY WELGHT: PATHOLOGIST: SID JONES, DUM, PHD, DACUP 1: 95 STUDY WEEK OF DEATH: 14 PROSECTOR: BARBARA DAY DOSE GROUP: 4 STUDY DAY OF DEATH: 95 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL DATE AND TIME OF NECROPSY: 07/14/86 13:52 DATE OF DEATH: 07/14/86 ANIMAL NUMBER: B08487

IINAL BODY WEIGHT: 431.0 GRAMS RECORDER: SID JONES, DUM, PHD, DACUP WETGHER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

CLINICAL DBSERVATIONS

-NEPHROPATHY, CHRONIC PROGRESSIVE,-HISTOPATHOLOGY -GRANLLAR CASTS, -SLIGHT KIDNEY (KD): MINIM **OBSERUATIONS** > NOTE: > EXTERNAL OBSERVATIONS: RIGHT EYE-CHROMODACRYORRHEA, NOSE-BLOODY *COLLECTED/IAKEN (XW) :
-ELECTRON MICROSCOPY SAMPLE; LIVER -PELUIS, DILATED) LEFT, SLIGHTLY GENERAL INFORMATION (XX): NECROPSY PATHOLOGY KIDNEY (KD): CRUST -RIGHT EYE-CHROMODACRYORRHEA; NOSE-BLOODY

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRIA, THORACIC (AD), BONE, FEMUR (FE), BONE, STERRUM (SB),
BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORO, CERUICAL (CS), CORD, LUMBAR (LC), CORO, THORACIC (TC),
BODDENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), LACRIMAL GI, EXO (EU),
LIVER (L1), LN, MESENTERIC (MS), LN, OTHER (LN), LUMG (LU), MAMMARY GLAND (MS), MAND SALTUARY GI (SG),
MASCLE, SKELETAL (SM), NERUE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI),
PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS), SPIEFN (SP), STOMACH, GI (SI),
STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), TRACHEA (TR), URINARY BLADDER (UB) THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRIA, THORACIC (AD), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN WASTEM (BR), CECUM (CE), COLON (CD), CORO, CERUICAL (CS), CORO, LUMBAR (LC), CORO, THORACIC (TC),
DUDDOENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), FYE (EY), HEART (HI), II FUM (IL), JEUNUM (JE), LAGRIMAL (E),
LIUGR (LI), LN, MESENTERIC (MS), LUNG (LU), MAMMARY GLAND (MS), MAND SALIUARY GL (SG), MARROLL, STERNUM (SE),
MUSCLE, SKELETAL (SM), NERUE, SCIATIC (SN), PANCREAS (PA), PARAHYROID (PI), PIULTARY (PI), PRUSTATE (PR),
RECTUM (RE), SEMINAL UESICLE (SU), SKIN (SK), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NORISL (SID), TESTIS (TE),
THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLANDER (UR) FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCIPIC EXAMINATION: 포

A** PATH/IN SYSTEM DUTPLI *** SUBCHRONIC TOXICITY STUDY IN RATS

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INDIVIDUAL ANIMAL SIMMARY REPORT

STUDY NUMBER: 2399108

SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE	TERMINAL BODY WEIGHT: 374.9 GRAMS	RECORDER: SID JONES, DUM, PHD, DACUP	PATHOLOGIST: SIO JONES, DUM, PHD, DACUP WEIGHER: NOT REQUIRED BY PROTOCOL
SACRIFICE STATUS:	K OF DEATH: 14	1.1	PATHOLOGIST: SID JONES, DUM, PHD, DACUP
DOSE GROUP: 4	STUDY DAY OF DEATH: 96 . STUDY WEEK OF DEATH: 14	PROSECTOR: TIM GROUE	
SEX: MALE	STUDY DAY OF D	07/15/86 9:07	JIRED BY PROTOCOL
ANIMAL NUMBER: B08488	DATE OF DEATH: 07/15/86	DATE AND TIME OF NECROPSY: 07/15/86 9:07	POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

! ! ! !	-	f
- APPEARED NORMAL	KIDNEY (KD): -PELUIS, DILATED; BOTH, MODERATELY -PELUIS, FLUID; RIGHT, MILKY -PELUIS, GRANULAR MATERIAL; BOTH, MHITE, PINPOINT -COLLECTED/TAKEN (XW); -ELECTRON MICROSCOPY SAMPLE; LIVER GENERAL INFORMATION (XX); >NOTE:>EXTERNAL OBSERVATIONS:NOME	KIDNEY (KD): -PELUIS, DILATATION,-MODERATELY SEVERE -PYELONEPHRITIS,-MODERATELY SEVERE -LUNG (LU): -PERIPRINCHIAL/PERIVASCUI AR, INFILTRATION, LYMPHOTO,-SI IGHT MARROW, STERNIM (SE): -HYPERCELLILAR,-MODERATE PROSTATE (PR): -INFLAMMATION, CHRONIC ACTIVE,-MODERATE SENINAL VESICIE (SV): -INFLAMMATION, CHRONIC ACTIVE,-MODERATE SENINAL VESICIE (SV): -INFLAMMATION, CHRONIC ACTIVE,-MODERATE SIRITARRY BLADDER (18): -CALCULUS,-PRESENT -MILCOSAL HYPERPLASIA,-SEVERE

APPENDIX 8 *** PATH/TOX SYSTEM CUITPUT *** SUBCHRONIC TOXICITY STIJOY IN RATS

PRINTED: 12-MAY-88 PAGE: 261

STIENY NIMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

RECORDER: SID JONES, DUM, PHD, DACUP WEIGHER: NOT REQUIRED BY PROTOIDI TERMINAL BODY WEIGHT: 374.9 GRAMS SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE PATHOLOGIST: SID JONES, DUM, PHO, DACUP STUDY WEEK OF DEATH: 14 PROSECTOR: TIM GROUE DOSE GROUP: 4 STUDY DAY OF DEATH: 96 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL 9:07 SEX: MALE DATE AND TIME OF NECROPSY: 07/15/86 DATE OF DEATH: 07/15/86 NUMBER: B08488 ANI MAL

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AGRIA, THORACIC (AG), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN WYSTEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LLMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EY (EY), HEART (HT), ILEUM (IL), JECUMIM (JE), LACRIMAL AL, EXO (ED),
MAND SALUARY GL (SS),
MAND SALUARY GL (SS),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PAHUREAS (PA), PARATHYRUID (PT), PITUITARY (PI),
PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (SI),
STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR), IRRIMARY RIADDER (IR) THE FOLLOWING DRGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRIA, THORACIC (AD), BONE, FEMIR (FE), BONE, STERRUM (SB),
BRAIN MASTEM (BR), CECUM (CE), COLON (CO), CORD, CERUICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
BUDDENUM (DU), EPIDIOYMIS (EP), ESOPHAGUS (ES), FYE (EY), HEART (HI), HEIM (IL), DELHRUM (A), LACRIMAL GI, FXD (FR),
LIUER (LI), LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIUARY GI (SG), MISCLE, SKELETAL (SM),
NERUE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PI), PITUITARY (PI), RECITM (RE), SKIN (SR), SALEEN (SP),
STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR) FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: 포

*** ALL DRGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/TOX SYSTEM OUTPUT *** APPENDIX 8

PRINTED: 12-MAY-88

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

TERMINAL BODY MEIGHT: 373.1 GRAMS RECORDER: SID JONES, DUM, PHD, DACUP WEIGHER: NOT REQUIRED BY PROTOCOL. SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE PATHOLOGIST: SID JONES, DUM, PHD, DACUP STUDY WEEK OF DEATH: 14 PROSECTOR: DOUGLAS HERNDON DOSE GROUP: 4 STUDY DAY OF DEATH: 96 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL DATE AND TIME OF NECROPSY: 07/15/86 10:34 SEX: MALE DATE OF DEATH: 07/15/86 ANIMAL NUMBER: 808489

*** ANIMAL HAS NO DRGAN WEIGHTS RECORDED ***

INFILTRATION, LYMPHOID, -SLIGHT -PERTERENCHIAL/PERTUASITAL AR HISTOPATHOLOGY PARATHYROID (PT) : 100 CLD : OBSERUATIONS -ELECTRON MICROSCOPY SAMPLE; LIUFR VNOTE: VEXTERNAL DBSFRUATIONS: NITNE ŧ GENERAL INFORMATION (XX): 1 NECROPSY *COLLECTED/TAKEN (XW) : PATHOLOGY THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY: CLINICAL DBSERUATIONS -APPEARED NORMAL

SECTION EXAMINED; TISSUE NOT PRESENT

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRIA, THORACTC (AD), BONE, FEMUR (FE), BUNE, STERNIM (SB),
BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORD, CFRUTCAL (CS), CORD, LUMBAR (LC), CORD, THORACTC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXD (ED), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUMG (LI), MAMMARY GLARD, (MS),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERUE, SCIATIC (SN), PANCREAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTIM (RE), SPMINAL UTSICLE (SU), SKIN (SC), SKIN, OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB)

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ANRIA, THORACIC (AU), BONE, FEMIR (FE), BONE, STERNIM (SR), BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC), DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), FYE (EY), HEART (HT), II FIN (IL), AFAINAUM (LF), KIDHFY (KD), LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), MAMMARY GLAND (MS), MAND SAI IVARY GI (SB), MUSCLE, SKELETAL (SM), NFRUE, SCIATIC (SM), PARICHEAS (PA), PITHITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NUMBL (SH), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (18) FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: 뿔

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOTINE) WERE SAVED ***

APPENDIX B *** PATH/TOX SYSTEM OUTPUT *** SUBCHRONIC TOXICITY STUDY IN RATS

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STILDY NUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: B08490 SEX: MALE DATE OF DEATH: 07/14/86 STUDY DAY OF DATE AND TIME OF NECROPSY: 07/14/86 14:54 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL	F DEATH	DOSE GROUP: 4 SACRIFICE STATUS: 1: 95 STUDY WEEK OF DEATH: 14 PROSECTOR: BARBARA DAY PATHOLOGIST: SID JONES, DUM, PHO, DACUP	SCHE	SCHFOLLED, TERMINAL SACRIFICE TERMINAL BODY WEIGHT: 405.0 SRAMS RECORDER: SID JONES, DUM, PHD, DACUP WEIGHER: BARBARA DAY	
ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN MEIGHT RATIO	ORGAN	11
ADRENAL (AD)	. 046	. 0114 %	.0232	MEIGHT TAKEN MEIGHT TAKEN	
HT)	1.03	25.5	. 350	MEJGHT TAKEN MEJGHT TAKEN	
KIDNEY (KD) LIVER (LI)	2.96	2,592 %	1.487		
TESTIS/EPIDIO (TP)	4.51	1.114 %	2.263	LIEUGHT TAKEN	i !
CLINICAL OBSERVATIONS	G G	HOLOGY OBSERUATIONS NECROPSY	SNB	нізтаратнацаву	i [
-APPEARED NORMAL	GENERAL INFOR	GENERAL INFORMATION (XX); >HOTE:>EXTERMAL ORSERVATIONS:NOWE	LIVER (LI): - (MR.TI)FOCS LUMG (LID): -PFRIREINCH INFILTRATI	UER (LI): - (MILI)FOCAL NECROSIS,-MODERATE - (LID): - PERIPAGNICHIAL/PERIVASIUM AR, INFILTRATION, LYMPHOIO,-MINIMAL	i

APPENDIX 8 *** PATH/TOX SYSTEM OUTPUT *** SUBCHRONIC TOXICITY STUDY IN RAIS

PRINTED: 12-MAY-RR PAGE: 264

STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

TERMINAL BODY MEIGHT: 405.0 GRAMS
RECORDER: SID JONES, DUM, PHD, DACUP SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE WEIGHER: BARBARA DAY PATHOLOGIST: SID JONES, DUM, PHD, DACUP STIJDY WEEK OF DEATH: 14 PROSECTOR: BARBARA DAY DOSE GROUP: 4 STUDY DAY OF DEATH: 95 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL DATE AND TIME OF NECROPSY: 07/14/86 14:54 DATE OF DEATH: 07/14/86 ANIMAL NUMBER: B08490

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AURTA, THORACIC (AD), RINE, FEMIR (FF), BONE, STERNIM (SB), BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORO, THURACIC (TC), DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), HEIM (LL), AGUNIM (GF), KIDNEY (KD), LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MS), MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MISCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PARTREAS (PA), PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NOMIGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), ACOLLECTED/TAKEN (XW) THE FOLLOWING ORGANS WERE LINREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AH), ADRIA, THORACIC (AD), BONE, FEMUR (FE), BINKE, STERNIM (SB), BRAIN W/STEM (BR), CECUM (CE), COLON (CD), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC), DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEARI (HI), ILEIM (IL), JEJHNIM (JE), KIDHEY (KD), LACRIMAL GL, EXO (EO), LN, MESENTERIC (MS), MAMMARY GLAND (MS), MAND SALIVARY GL (SG), MARROLM, STERNUM (SE), MUSCLE, SKELETAL (SM), NERUE, SCIATIC (SN), PANCREAS (PA), PARATHYRUJO (PI), PITHITARY (PI), PROSTALE (PR), RECTUM (RE), SEMINAL WESICLE (SU), SKIN (SK), SPLEEN (SP), STOMACH, GL (SI), STOMACH, NONGL (SH), TESTIS (TE), THYMUS (TH), THYRUJO (TY), TRACHEA (TR), URINARY BLADDER (HB) THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/TIN SYSTEM CUIPUT *** APPENDIX 8

PRINTED: 12-MAY-88 PAISE: 265

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

287.1 GRAMS TERMINAL BODY WEIGHT: 26 RECORDER: BARBARA DAY SACRIFICE STATUS: UNSCHEDULED (D) PATHOLOGIST: NOT REQUIRED BY PROTOCOL 4: 56 STJDY WEEK OF DEATH: 8 PROSECTOR: BARBARA DAY DOSE GROUP: 4 STUDY DAY OF DEATH: 56 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL 7:45 DATE OF DEATH: 06/05/86 STUDY (
DATE AND TIME OF NECROPSY: 06/05/86 ANIMAL NUMBER: B08491

WEIGHER: NOT REQUIRED BY PRINTENCIAL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

CLINICAL OBSERVATIONS

-APPEARED NORMAL

PATHOLOGY OBSERVATIONS NECROPSY

ALL LOBES, LIGHT TO DARK RED (ST): -MOTTLED; ALL LOBES, LIGHT TO DARK RESTONACH, GL (ST):
-PALE AREA; FUNDIC MUCOSA, SEVERAL,
LINEAR, WHITE, 4 X 2 MM TO 1.0 X 0.2 LUNG (LU): -FAILURE TO COLLAPSE; ALL LOBES

GENERAL INFORMATION (XX):
>NOTE:>LAST IN-LIFF AND EXTERNAL OBSERVATIONS: NONE

HISTOPATHOLOGY

-FORETGN BODY PNEUMONIA, -MODERATE

-INFLAMMATION, CHRONIC,-MINIMAL

PANCREAS (PA):

CONG CLED :

STOMACH, GL. (ST):

APPENDIX B *** PATH/IDX SYSTEM DUTPUT ***

*** PRINZIUX SYSTEM (UNIFUL *** SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88

INDIVIDUAL ANTMAL SUMMARY REPORT

STIDY NIMBER: 2399108

WEIGHER: NOT REQUIRED BY PRINTORO 287.1 GRAMS TERMINAL BODY WEIGHT: 21 RECORDER: BARBARA DAY SACRIFICE STATUS: UNSCHEDULED (D) PATHOLOGIST: NOT REDUIRED BY PROTOCOL STUDY WEEK OF DEATH: 8 PRUSECTOR: BARBARA DAY DOSE GROUP: 4 DATE OF DEATH: 06/05/86 STUDY DAY OF DEATH: 56
DATE AND TIME OF NECROPSY: 06/05/86 7:45 PRUSE POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL SEX: MALE DATE OF DEATH: 06/05/86 ANIMAL NUMBER: B08491

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRIA, THORACIC (AD), BITHE, FEMINE (FE), ROME, STERNIM (SB),
BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEIM (IL), AFARIMIM (JE), KIOHFY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), MAMMARY GLAND (MG), MAND SAI LUARY GI (SG),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA), PARATHYRNID (PT), PITUITARY (PI),
PROSTATE (PR), RECTUM (RE), SEMINAL UESICLE (SU), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, NONGL (SB),
TESTIS (TE), THYMUS (TH), THYRDID (TY), TRACHEA (TR), URINARY BLADDER (18), "COLLECTED/TAKEN (XM) THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

PROSTALE (PR), ADRENAL, CORTEX (AC), ADRENAL, MEDILLA (AM), ADRIA, THORAGIC (AD), BONE, FEMIR (FE), BONE, STERNIM (SB), BRAIN MASTEM (RC), CORD, LUMBAR (LC), CORD, THORAGIC (TC), BRAIN MASTEM (B), CECUM (CE), CORD, CECUM (CE), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORAGIC (TC), DUODENUM (DU), EPIDIOYMIS (EP), ESOPHAGUS (FS), EYE (EY), HEART (HT), ILEUM (IL), GRINIMA (AF), KIDNEY (KD), LACRIMAL GL, EXO (EO), LIVER (L1), LN, MESENTERIC (MS), MAMMARY GLAND (MS), MAND SALIDARY GI (SG), MASCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PARATHYRRID (PT), PITHITARY (PI), PROSTALE RECTUM (RE), SEMINAL WESICLE (SV), SKIN (SK), SPLEEN (SP), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (IB) THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

*** ALL ORGANS/TISSUES (REDUIRED TO BE HARVESTED PER THE STIIDY PROTOCOL) WERE SAVED ***

SUBCHROWIC TOXICITY STUDY IN RATS *** PATH/TOX SYSTEM DUITPUT *** APPEND1X 8

PRINTED: 12-MAY-88 PAGE: 267

INDIVIDIJAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399100

TERMINAL BUDY MEIGHT: 435.9 GRAMS RECORDER: SID JONES, DUM, PHD, DACUP 435.9 GRAMS SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE PATHOLOGIST: SID JONES, DUM, PHD, DACUP 1: 96 STUDY MEEK OF DEATH: 14 PROSECTOR: DOUGLAS HERNDON DOSE GRUUP: 4 STUDY DAY OF DEATH: 96 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL DATE AND TIME OF NECROPSY: 07/15/86 11:35 DATE OF DEATH: 07/15/86 ANIMAL NUMBER: B08492.

WEIGHER: NOT REQUIRED BY PROTOTON

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

CLINICAL OBSERVATIONS

-APPEARED NORMAL

PATHOLOGY OBSERVATIONS NECROPSY

-ELECTRON MICROSCOPY SAMPLE; LIUER ANDTE: VEXTERNAL DBSERVATIONS: NOME GENERAL INFORMATION (XX) : COLLECTED/TAKEN (XW) :

INFILTRATION, LYMPHOID, -SLIGHT -PERIBRONCHIAL/PERIVASCULAR . G.D. SHI

-NEPHRAPATHY, CHRONIC PROGRESSIVE,-

KIDNEY (KD):

MINIM

HISTIJPATHOLOGY

ADRENAL, CORTEX (ACT), ADRENAL, MEDULLA (CA), ADRIA, THORACIC (AD), BONE, FEMUR (FE), BONE, STERNUM (SB), BRENAL, CORTEX (AC), ADRENAL, CORTEX (AC), CORO, THORACIC (TC), BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORO, THORACIC (TC), BUDDOENUM (DU), EPIDIDYMIS (EP), ESDHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIONEY (KD), LACRIMAL GL, EXD (EO), LIVER (LI), LN, MESENTFRIC (MS), LN, OTHER (LN), LUMG (LI), MAMMARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTIM (RE), SEMIHAL UESICE (SU), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB) THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRIA, THÉRACIC (AD), BRUNE, FEMUR (FE), BONE, THÜRACIC (TE),
BRAIN WSTEM (BR), CECUM (CE), COLON (CO), CORO, CORO, LUMBAR (LE), CORO, THÜRACIC (TE),
BUODENUM (DU), EPIDIDYMIS (FP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILFIM (LE), REJINUM (JE), LARRINGE, SKELETAL (FD),
LIVER (LI), LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SS), MARROW, STERNUM (SE), MISCLE, SKELETAL (SM),
NERUE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PT), PITHITARY (FI), PRINSIALE (FR), RECTUM (RE),
SEMINAL VESICLE (SU), SKIN (SK), SPLEEN (SP), SIOMACH, GL (ST), STOMACH, NOWGL (SU), TESTIS (TE), THYMIS (TH),
THYROID (TY), TRACHEA (TR), URINARY BLADDER (HB) FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: 표

*** ALL DRGANS/TISSMES (REQUIRED TO BE HARVESTED PER THE STROY PROTOCAL) WERE SAUFD ***

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/TOX SYSTEM DUTPUT *** APPENDIX 8

PRINTED: 12-MAY-88 PAISE: 263

INDIVIDUAL ANIMAL SLIMMARY REPORT

STUDY NUMBER: 239910R

317.0 GRAMS TERMINAL BRIDY WEIGHT: RECORDERS TIM GROUE SACRIFICE STATUS: UNSCHEDULED (D) PATHOLOGIST: NOT REQUIRED BY PROTOCOL H: 17 STUDY WEEK OF DEATH: 3
PROSECTOR: TIM GROVE DOSE GROUP: 4 DATE OF DEATH: 04/27/86 STUDY DAY OF DEATH: 17
DATE AND TIME OF NECROPSY: 04/27/86 13:47 PROSE POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL SEX: MALE DATE OF DEATH: 04/27/86 ANIMAL NUMBER: 808493

WEIGHER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

		\$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ 1 1 1 1 1 1 1 1 1
CLINICAL OBSERVATIONS	PATHOLOGY OBSERUATIONS NECROPSY	HISTOPATHOLOGY
-APPEARED NORMAL	LUNG (LU): -FAILURE TO COLLAPSE; ALL LURES -MOTTLED; ALL LOBES, TAN TO DARK RED GENERAL INFORMATION (XX): >NOTE:>LAST IN-LIFE AND EXTERNAL DBSERVATIONS:CONVULSIONS, FOUND	LUNG (LU): -PFRIERCHCHIAL/PFRIUASCULAR, INFILTRATION, LYMPHDIO,-SIIGHT -CONSESTIEM,-MODERATE -FOREIGN MATERIAL,-PRESENT MANMARY GLAND (MS):
	1 1 1 1 1 1 1	COCKETTON EVALUATION OF THE PARTY AND A SECOND OF THE PARTY AND A SECO

SENT

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRIA, THORACIC (AD), BONE, FEMUR (FE), BONE, STERNIM (SB),
BRAIN WASTEM (BR), CECUM (CE), COLON (CA), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNIM (JE), KIONEY (KD),
LACRIMAL GL, EXO (ED), LIVER (LI), LN, MESENTERIC (MS), IN, OTHER (IN), MAMMARY GLAND (MG), MAMD SALIVARY GL (SA),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PT), PITHITARY (PI),
PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS), SPLEFN (SP), STOMACH, GL (ST),
STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), ACCILECTED/TAKEN (XM) THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

MUSCLE, SKELETAL (SM), NERUE, SCIATIC (SN), PANCREAS (PA), PARATHYRGIO (PI), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SU), SKIN (SK), SPLEFN (SP), STOMACH, RL (SI), STOMACH, NOWSL (SU), TESTIS (TF), THYMUS (TH), THYRGID (TY), TRACHEA (TR), URINARY BLADDER (UR) ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AURTA, THORACIC (AD), BONE, FEMIR (FE), BONE, STERRIM (SR), BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CRUTCAL (CS), CORD, LIMBAR (LC), CARD, THORACIC (TC), DUDDENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (LL), JEJINNUM (JE), KIONEY (KD), LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), MAND SALIVARY (SI (SG), MARKIM, SIFRNUM (SE), FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: 포

*** ALL ORGANSZIISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTICIO) LARGE SAUFD ***

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/TOX SYSTEM DUTPUT *** APPENDIX B

FR]NTED: 12-MAY-88 PAGE: 269

INDIVIDIAL ANIMAL SUMMARY REPORT

STUDY MIMPER: 2399108

TERMINAL BODY WEIGHT: 415.0 GRAMS RECORDER: SID JONES, DUM, PHD, DAILUP SACRIFICE STATUS: SCHEDULFD, TERMINAL SACRIFICE PATHOLOGIST: SID JONES, DUM, PHD, DACUP STUDY WEEK OF DEATH: 14 PROSECTOR: BARBARA DAY DOSE GROUP: 4 STUDY DAY OF DEATH: 97 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL DATE AND TIME OF NECROPSY: 07/16/86 9:10 SEX: MALE DATE OF DEATH: 07/16/86 ANIMAL NUMBER: 808494

WEIGHER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

HISTOPATHOLOGY CON SMOT PATHOLOGY OBSERVATIONS ^COLLECTED/TAKEN (XW) :
 -ELECTRON MICROSCOPY SAMPLE; LIVER NECROPSY CLINICAL DBSERUATIONS -APPEARED NORMAL

INFILTRATION, LYMPHOID, -SI IGHT -PERTHRONCHIAL/PERTUASCULAR ANDTE: SEXTERNAL OBSERVATIONS: NONE GENERAL INFORMATION (XX) :

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRIA, THARACIC (AD), BONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN WASTEM (BR), CECUM (CE), COLON (CD), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUDDENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JF), KIONEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MS),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICE (SU), SKIN (SK), SKIN, OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TF), THYMUS (TH), THYROID (TY), TRACHEA (TR), ŧ THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY: URINARY BLADDER (UB)

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AO), BONE, FEMIR (TE), BONE, SIFRNIM (SB),
BRAIN WASTEM (BR), CECUM (CE), COLON (CD), CORO, CERVICAL (CS), CORO, LUMBAR (LC), CORO, THORACIC (TC),
DUODENUM (DU), EPIDIOYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), HEIM (TL), JERNNIM CE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA), PARATHYRHO (PT), PITUTIARY (PD),
PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU),
TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHFA (TR), TRINARY BLADDER (UB) THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) MERE SAVED ***

A** PATH/TÜX SYSTEM DUITPUT *** SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-80 PAGE: 270

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399188

			CONTRACTO TOTAL	BULLETON MANTHOUT OF BESTINGS
ANIMAL NUMBER: 808495	SEX: MALE	DUISE GRUNDE: 4		SHENTILLE SINIIS STREETURE IS TERRITORI, SHENTILLE
DATE OF DEATH: 07/16/86	STUDY DAY OF DEATH: 97	ATH: 97 STUDY WEEK OF DEATH: 14	OF DEATH: 14	TERMINAL BODY WEIGHT: 406.3 GRAMS
DATE AND TIME OF NECROPSY: 07/16/86 10:13	07/16/86 10:13	PROSECTOR: BARBARA DAY	> -	RECORDER: SID JONES, DUM, PHD, C
POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL	IRED BY PROTOCOL	PATHOLOGIST: SID JONES, DUM, PHD, DACUP	S, DUM, PHD, DACUP	WEIGHER: NOT REQUIRED BY PROTOCO
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1S , DACUP

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

PATHOLOGY O CLINICAL DBSERVATIONS NECRO	PATHOLOGY OBSERUATIONS NECROPSY	
-APPEARED NORMAL	COLLECTED/TAKEN (XW): -ELECTRON MICROSCOPY SAMPLE; LIVER GENERAL INFORMATION (XX): >NOTE:>EXTERNAL OBSERVATIONS:NOWE	KIDNEY (KD): -MEPHRIPATHY, CHROMIC PROGRESSIUE,-MINIMAL FILMS (1.1): -PERTERROMCHIALZPERIUASCULAR, INFILTRATION, LYMPHOTO,-SLIGHT PARATHYROTO (PT): >SECTION EXAMINED; TISSIE NOT PRESENT

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/TOX SYSTEM DUITPLIT *** APPENDIX B

PRINTED: 12-MAY-88

STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

WEIGHER: NOT REQUIRED BY PROTOCOL 406.3 GRAMS SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE TERMINAL BODY OF IGHT! PATHOLOGIST: SID JONES, DUM, PHD, DACUP STUDY WEEK OF DEATH: 14 PROSECTOR: BARBARA DAY DOSE GROUP: 4 STIJDY DAY OF DEATH: 97 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL DATE AND TIME OF NECROPSY: 07/16/86 10:13 SEX: MALE DATE OF DEATH: 07/16/86 ANIMAL NUMBER: B08495

RECORDER: SID JONES, DUM, PHD, DACUP

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ANRIA, THORACIC (AD), BONE, FEMIRE (FE), BONE, STERNUM (SB),
BRAIN WASTEM (BR), CECUM (CE), CORO, CORO, CORO, LUMBAR (LC), CORO, THORACIC (TC),
BOUDDENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), DEJUMIN (JE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MS),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCIE, SKELETAL (SM), NERVE, SCIATIC (SN), PANGREAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMIS (TH), THYRDID (TY), TRACHER (TR), URINARY BLADDER (UB)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCIPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRIA, THORACIC (AD), BONE, FEMUR (FE), BONE, STERNIM (SB),
BRAIN WASTEM (BR), CECUM (CE), COLON (CD), CORD, CERUICAL (CS), CORD, LIMBAR (LC), CORD, THORACIC (TC),
DUDDENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JF), LACRIMAL G., EXD (ED),
LIVER (LI), LN, MESENTERIC (MS), MAMMARY GLAND (MS), MAND SALIVARY G. (SG), MARROW, STERBUM (SE), MISCLE, SKELFTAL (SM),
NERUE, SCIATIC (SN), PANCREAS (PA), PITUITARY (PI), PROSTATE (PR), RECTUM (RF), SEMINAL VESICLE (SU), SKIN (SK),
SPLEEN (SP), STOMACH, GL (SI), STOMACH, NONGL (SU), TESTIS (TE), THYMIS (TH), THYROID (TY), TRACHFA (TR), URINARY BLADDER (UB)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STHDY PROTOCOL) WERE SAVED ***

APPENDIX 8 *** PATH/TOX SYSTEM CLITPLIT *** SUBCHRONIC TOXICITY STUDY IN RATS

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	GINJONI	INDIVIDUAL ANIMAL SUMMARY REPORT		STIDY MUMBER: 2399188
ANIMAL NUMBER: 808496 SEX: MALE DATE OF DEATH: 07/15/86 STUDY DAY OF DATE AND TIME OF NECROPSY: 07/15/86 8:28 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL	DEATH	WEEK O ARA DAY D JONES	SCHE	DULED, TERMINAL SACRIFICE INAL BODY WEIGHT: 444.9 GRAMS RECTROBER: SID JONES, OUM, PHD, DACUP WEIGHER: BARBARA DAY
ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	DRGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN MEIGHT RATIO	ORGAN Status
! _	. 041	. 10091 %	. 11215	
BRAIN WYSTEM (BR) HEART (HT)	1.08 1.05	. 423 % . 235 %	1,000	LEIGHT TAKEN
SPLEEN (SP)	.63	.141 %	.334	WEIGHT TAKEN
	3,13	% ₹UZ.	1.662	LIFIGHT TAKFN
LIVER (LI)	13.02	2.926 %	6.924	LIFT GHT TAKEN
TESTIS/EPIDIO (TP)	4.39	% Z86.	2,335	MFIGHT TAKEN
CLINICAL DBSERUATIONS	PATHOLOS Y ONS	O G Y O B S E R U A T J	8 N O	HISTOPATHOLOGY
	111111111111111111111111111111111111111			
-APPEARED NORMAL	GENERAL INFO	GENERAL INFORMATION (XX): >NOTE:>EXTERNAL DRSERVATIONS:NONE	KIDNEY (KD): NEPHRIPATHY, CHRI MINIMAL LIME (LID): -PERIBRONCHIAL/PEI INFILTRATION, LYPEI INFILTRATION, LYPEI NAMMARY (1) AND (MS) > SECTION EXAMINED PARATHYROID (PT): > SECTION EXAMINED	DNEY (KD): -NEPHRIPATHY, CHRONIC PROGRESSIVE,- MINIMAL MS (LI): -PERIBRONCHIAL/PERIVASCULAR, INFILTRATION,-LYMPHOID,-SI IGHT MMARY (RAID (MS): -SECTION EXAMINED; TISSUE NOT PRESENT >SECTION EXAMINED; TISSUE NOT PRESENT >SECTION EXAMINED; TISSUE NOT PRESENT

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/10X SYSTEM OUTPUT *** APPENDIX 8

PRINTED: 12-MAY-88

INDIVIDUAL ANIMAL SUMMARY REPURT

STUDY NUMBER: 2399108

IINAL BODY WEIGHT: 444.9 GRAMS RECORDER: SID JONES, DUM, PHD, DACUP SACRIFICE STATUS: SCHEDULFD, TERMINAL SACRIFICE WE IGHER: BARBARA DAY TERMINAL BODY WEIGHT: PATHOLOGIST: SID JONES, DUM, PHO, DACUP STUDY WEEK OF DEATH: 14 PRISECTOR: RARBARA DAY DOSE GROUP: 4 STUDY DAY OF DEATH: 96 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL DATE OF DEATH: 07/15/86 STUDY DAY OF DATE AND TIME OF NECROPSY: 07/15/86 8:28 SEX: MALE ANIMAL NUMBER: 808496

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDILLA (AM), AGRIA, THORACIC (AD), BORE, FEMIR (FE), BORNE, STERBUM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORO, CERVICAL (CS), CORO, LUMBAR (LC), CORO, THURACIC (TC),
BOUDDENUM (DU), EPIDIOYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), HEUM (LL), GENHAUM (DE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUMG (LU), MAMMARY GLAND (MS),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), HERVE, SCIATIC (SN), PARICREAS (FA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NINGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR),
URINARY BLADDER (UB), COLLECTED/TAKEN (XM)

FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: 뽀

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRTA, THURACIC (AD), BONE, FEMUR (FE), BONE, STERNIM (SB),
BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORD, CERUICAL (CS), CORD, LIMBAR (LC), CORD, THURACIC (TC),
DUDDENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), LACRIMAL G., EXD (ED),
LIVER (LI), LN, MESENTERIC (MS), MAND SALIVARY GL (SB), MARROLL, STERNIM (SE), MUSCIE, SKFIETAL (SM),
NERUE, SCIATIC (SN), PANCREAS (PA), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SU), SKIN (SK),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

A** PATH/ITIX SYSTEM CHITPHT *** SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-89 PAGE: 274

	OINI GNI	INDIVIDUAL ANIMAL SUMMARY REPURT	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	STUDY NUMBER: 2399108
ANIMAL NUMBER: B08497 SEX: MALE DATE OF DEATH: 07/15/86 STUDY DAY OF DATE AND TIME OF NECROPSY: 07/15/86 11:37 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL	ОЕАТН	DOSE GROUP: 4 SACRIFICE STATUS: 18-96 STUDY WEEK OF DEATH: 14 PROSECTOR: BARBARA DAY PATHOLOGIST: SID JOHES, DUM, PHO, DACUP	SCHE	SCHFDURED, TERMINAL SACRIFITE TERMINAL BODY WEIGHT: 449,7 GRAMS RECORDER: SIO JUNES, IVM, FID, DAICH WEIGHER: BARBARA DAY
DRGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	DRGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORSAN TO BRAIN METGHT RATIO	O R G A N S T A T U S
ADRENAL (AD) BRAIN LINGTEM (BR)	. 056	. 0125 %	. n298	MIJEHT TAKEN
	1.00		- Pro- Pr	
SPLEEN (SP) KIDMEY (KD)	3.27	第一元の17 第一元の17 第一元の17	1.798	WF 1541 THREE UITEN TOWEN
LIVER (LI) TESTIS/EPININ (TP)	11.32	2.518 %	5.984 2.630	METGHT TAKEN METGHT TAKEN
	T & G	HOLOGY OBSERUATIONS NECROPSY	;	
-APPEARED NORMAL	GENERAL LINE	GENERAL INFORMATION (XX): >NOTE:>EXTERNAL OBSERVATIONS:NOBE	LUNG (LU): - PERTINGULUH INFILTRATI PRISSTATE (PR - MONONICLEA	LUNG (10): -PERTENDICHTALZPERTUASCHLAR, INFLLTRATION, LYMPHOID,-SLIGHT PRESTATE (PR): -MONONLICLEAR CELL INFILTRATE,-SLIGHF

APPENDIX 8 *** PATH/TOX SYSTEM CUITPLI *** SUBCHRONIC TOXICITY STIDY IN RATS

PRINTED: 12-MAY-BE PAGE: 275

STUDY HUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

TERMINAL BODY MEIGHT: 449.7 GRAMS RECORDER: SID JONES, DUM, PHD, DACUP SACRIFICE STATUS: SCHFOULFD, TERMINAL SACRIFICE WEIGHER: BARBARA DAY PATHOLOGIST: SID JONES, DUM, PHD, DACUP STUDY WEEK OF DEATH: 14 PROSECTOR: BARBARA DAY DOSE GROUP: 4 STUDY DAY OF DEATH: 96 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL DATE AND TIME OF NECROPSY: 07/15/86 11:37 SEX: MALE DATE OF DEATH: 07/15/86 ANIMAL NUMBER: B08497

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AGRIA, THORACIC (AD), HOME, FEMIR (FE), BOWE, STERNUM (SB),
BRAIN WSTEM (BR), CECUM (CE), COLON (CO), CORO, CERVICAL (CS), CORO, LUMBAR (LC), CORO, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESDPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (LU), MAMMARY GLAND (MG),
LACRIMAL GL, EXO (ED), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG),
HAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCIE, SKELETAL (SM), NERVE, SCIATIC (SN), FARISREAS (PA),
PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL DESICLE (SV), SKIN (SK), SKIN, OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMIS (TH), THYROID (TY), TRACHER (TR),
URINARY BLADDER (UB), ACOLLECTED/TAKEN (XW)

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ANRIA, THORACIC (AN), BONE, FEMUR (FE), BONE, STERRUM (SB),
BRAIN WASTEM (BR), CECUM (CE), COLON (CN), CHROLC (CS), CORD, LIMBAR (LC), CORD, THIRACLC (TC),
DUDDENUM (DI), EPIDIDYMIS (EP), ESDPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD),
LACRIMAL GL, EXO (ED), LIVER (LI), LN, MESENTFRIC (MS), MAMMARY GLAND (MS), MAND SALIVARY GL (SS),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERUE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI),
RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SPLEEN (SP), STOMACH, RL (ST), STOMACH, MURSL (SU), 1ESTIS (IF),
THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB) FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: 뽀

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

APPENDIX 8 *** PATH/TOX SYSTEM DUTPUL *** SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

5

SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE	TERMINAL BODY WFIGHT: 451.3 GRAMS	RECORDER: SID JONES, DUM, PHD, DACU	WEIGHER: NOT REQUIRED BY PROTOCOL
TATUS:			DACUP
S BUI	H: 14		₽.
SACRIE	: DEAT		, DOM,
DOSE GROUP: 4	97 STUDY WEEK OF DEATH: 14	PROSECTOR: BARBARA DAY	PATHOLOGIST: SID JONES, DUM, PHD, DACUP
SEX: MALE	STUDY DAY OF DEATH: 97		
ANIMAL NUMBER: 808498	DATE OF DEATH: 07/16/86	DATE AND TIME OF NECROPSY: 07/16/86 11:22	POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

SULFINE CREEKATIONS	PATHOLOGY OBSERUATIONS NECROPSY	HISTOPATHOLOGY
1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	
-APPEARED NORMAL	^COLLECTED/TAKEN (XW) :	CUMS (LU) :
	-ELECTRON MICROSCOPY SAMPLE; LIUFR	-PERTERNACHIAL/PERIUASCULAR,
	GENERAL INFORMATION (XX):	INFILTRATION, LYMPHOID, -SLIGHT
	>NOTE:>EXTERNAL DESERVATIONS:NOTE	MANMARY SI AND (MS) 1
		SECTION EXAMINED; TISSUE NOT PRESEN
THE FOLLOWING ORGANS WERE UNREMARKABLE AT	E AT NECROPSY:	
ADDENAL CODIEX (AC) ADDENAL MEDITLI	THE LAW ADDITE THOOPILE (AD) BONE FEMING (FF) BONE STERNING (SB)	FF) BONE STERNIN (SR)

Ę

BRAIN W.STEM (BR), CECUM (CE), COLON (CO), CORD, FERUICAL (CS), CORD, FLWBAR (LC), CORD, THORACIC (TC), BONE, SERVICAL (CS), CORD, FERUIN (LC), CORD, THORACIC (TC), DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (LL), JEJUNIM (JC), KIDNEY (KD), LACRIMAL GL, EXO (EO), LIVER (LT), LN, MESENTERIC (MS), LN, MINER (LN), FING (LN), MANIMARY SI AND (MS), MAND SALIUARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NFRUE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTIM (RE), SEMIMAL VESICE (SU), SKIN (SK), SKIN, MINER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR),

ABRENAL, CORTEX (AC), ADRENAL, MEDILLA (AM), ADRIA, THORACIC (AD), BUNE, FFMIR (FF), BONE, STERNIM (SB), BRAIN WASTEM (BR), CECUM (CE), COLON (CD), CORD, CERVICAL (CS), CORD, LLMBAR (LC), CORD, THORACIC (TC), DUODENUM (DU), EPIDIOYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEARI (HI), HEIM (IL), AELINHIM CIF), KIDHEY (KD), LOODENUM (DU), EPIDIOYMIS (ED), LIVER (LI), LN, MESENTERIC (MS), MAND SALIVARY GL (SG), MERROW, STERNUM (SF), MUSCLE, SKELETAL (SM), NERUE, SCIATIC (SN), PANCREAS (FA), PARATHYRUID (FT), PITHITARY (PI), PRISTATE (FR), RECTUM (RE), SEMINAL VESICLE (SU), SKIN (SK), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NINGL (SU), TESTIS (TF), THYMUS (TH), THYROID (TY), TRACHEA (TR), URTHARY BLADDER (HB) FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: 뽀

ALL DRGANS/TISSUES (REQUIRED TO BE HARVESTED FER THE STUDY PROTOCOL) WERE SAVED ***

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/TOX SYSTEM DUTPUT *** APPENDIX 8

PRINTED: 12-MAY-88 PAGE: 277

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NIMBER: 2399108

SACRIFICE 1: 433.5 GRAMS TERMINAL BIRDY MEIGHT: SACRIFICE STATUS: SCHEDULED, TERMINAL PATHOLOGIST: SID JONES, DUM, PHD, DACUP STUDY MEEK OF DEATH: 14 PROSECTOR: BARBARA DAY DOSE GROUP: 4 STUDY DAY OF DEATH: 97 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL DATE OF DEATH: 07/16/86 STUDY DAY OF DATE AND TIME OF NECROPSY: 07/16/86 12:11 ANIMAL NUMBER: B08499

RECORDER: STO JONES, DUM, PHD, DAILUP WETCHER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

	PATHOLOGY DBSERUALINGS	VOC WISTOPOLICE
CLINICAL DBSERVATIONS	NEL/KUPSI	
-APPEARED NORMAL	^COLLECTED/TAKEN (XW) :·	CITING (LET)
	-ELECTRON MICROSCOPY SAMPLE; LIVER	-PFRIERFRENIA ZFRIGASILII AK,
	GENERAL INFORMATION (XX):	INFILTRATION, LYMPHOID, -SLIGHT
	>NOTE:>EXTERNAL DESERVATIONS:NOME	MAMMARY ELAND (MS):
		SECTION EXAMINED; TISSUE NOT PRESENT
1 1 1 1 1 1		
THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:	OLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:	
	- CINCL Liste 1600 Cick Cick 48001 1511 15	

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORIA, THORACIC (AD), BINE, FEMIR (FE), BORE, STERMIM (SR), BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CORD, LUMBAR (LC), CORD, THORACIC (TC), DUDDENUM (DU), EPIDIDYMIS (FP), ESOPHAGUS (ES), FYE (EY), HEART (HI), IFELM (II), DELINAM (AC), KICHEY (KD), LACRIMAL GL., EXD (EO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNS (LU), MAMMARY GLAND (MG), MAND SALIVARY GLASS, MARROW, STERNUM (SE), MUSICLE, SKELFIAL (SM), NERVE, SCIATIC (SM), PARTIFFAS (FA), PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE); SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, MONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB)

MUSCLE, SKELETAL (SM), NERUE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SU), SKIN (SK), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NOWSL (SU), TESTIS (TF), THYMUS (TY), TRYROID (TY), TRACHEA (TR), URINARY BLADDER (IB) ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AD), BONE, FEMUR (FE), BONE, STERBUM (SB), BRAIN WYSTEM (BR), CECUM (CE), COLON (CO), CORO, CERUICAL (CS), CORD, LIMBAR (LC), FORD, THORACIC (TC), DUDDENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HI), (LEUM (IL), JEJUNUM (JF), KIDNEY (KD), LACRIMAL GL, EXD (EO), LIUER (LI), LN, MESENTERIC (MS), MAND SALIUGARY SI (SG), MARROLL, SIERBUM (SF), THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTUCOLD MERE SAUFD ***

APPENDIX 8 *** PATH/TOX SYSTEM OUTPUT *** SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88 PAISE: 278

STUDY NUMBER: 9399188

INDIVIDUAL ANIMAL SUMMARY REPORT

	ABCOLLETE OBCON METCHT	DREAN METCHT RELATIVE	DOCAN TO BRAIN	X & C & C
ORGAN NAME	(GRAMS)	TO BODY WEIGHT (%)	METGHT PATIO	STATUS
ADREMAL (AD)	. 052	.0117 %	. 11243	WEIGHT TAKEN
BRAIN W/STEM (BR)	2.14	.483 %	1.000	LETGHT TAKEN
HEART (HT)	1.10	. 248 %	.514	LIFTGHT TAKEN
SPLEEN (SP)	.91	.205 %	. 425	METCHT TAKEN
KIDNEY (KD)	3.24	. 731 %	1.514	LIFTGHT TAKEN
LIVER (LI)	14.54	3.279 %	6.794	WEIGHT TAKEN
TESTIS/EPIDID (TP)	5.40	1.218 %	2.593	WEIGHT TAKEN
*	P A T H O L	HOLOGY OBSERVATIONS	5 Z	; † ! † † †
CLINICAL DBSERUATIONS		NECROPSY		HISTOPATHOLOGY
-APPEARED NORMAL	LIUER (LI): -RAISED ARE; -RAISED ARE; TAN, DARK (>NOTE;>DARK (>NOTE;>DARK (>NOTE;>EXTER	UER (LI): -RAISED AREA; LEFT LATERAL LÜGE, ÜWE, TAN, DARK RED, 8 X 5 MM >NOTE:>DARK AREA, PÜSSIR! E INJECTIRN SITE NERAL INFORMATION (XX): NOTE:>EXTERNAL GÜSSERUATIGNS:NOME		UER (LI): - INJECTION SITE; - PRESENT - NATCTION SITE; - PRESENT - PRESENCHIALZPERIUASCUI AR; - INFILTRATION; LYMPHOIO; - MINIMAL RATHYROID (PI): > SECTION EXAMINED: 115SME NOT PRESENT

APPENDIX 8 *** PATH/IOX SYSTEM OUTPUT *** SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88 PAGE: 279

INDIVIDUAL ANIMAL SUMMARY REPORT

ST102 MIMBER: 2599108

RECORDER: SID JONES, DUM, PHD, DACUP 443.4 GRAMS SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE WEIGHER: BARBARA DAY TERMINAL BODY METCHT: PATHOLOGIST: SID JONES, DUM, PHD, DAIJUP STUDY WEEK OF DEATH: 14 PROSECTOR: BARBARA DAY DOSE GROUP: 4 STUDY DAY OF DEATH: 97 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL 8:20 SEX: MALE DATE AND TIME OF NECROPSY: 07/16/86 DATE OF DEATH: 07/16/86 ANIMAL NUMBER: B08500

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AGRIA, THORACIC (AD), BRUE, FEMIR (FE), BORE, STERNUM (SB),
BRAIN W.STEM (BR), CECUM (CE), COLON (CO), CORD, CERUICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEDIMHUM (JF), KIDNEY (LD),
LACRIMAL GL, EXO (EO), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LD), MAMMARY GLAND (MG), MAND SALIVARY GL (SG),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERUE, SCIATIC (SN), PANCREAS (PA), PARATHYROID (PT), PITHITARY (PI),
PROSTATE (PR), RECTUM (RE), SEMINAL UESICLE (SV), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST),
STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR), HRIMARY BLADDER (118), ACRUIECTIFD/TAKEN (XM) THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDILLA (AM), ADRIA, THORACIC (AD), BINE, FFMIR (FE), RONE, STERNUM (SB), BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORO, CERVICAL (CS), CORO, LUMBAR (LC), CORO, THORACIC (TC), DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGIS (ES), FYE (EY), HEART (HT), ILEIM (IL), JEJINIM (JF), KIDMFY (KD), LACRIMAL GL, EXD (EQ), LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SF), MUSCLE, SKELETAL (SM), NERUE, SCIATIC (SN), PANCREAS (PA), PILLITARY (PI), PRISTATE (PR), RECTUM (RF), SEMINAL UESICLE (SU), SKIN (SK), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), TESTIS (TE), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (IR) THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOTOR) JUFFE SAVED ***

A** PATH/TOX SYSTEM OUTPUT *** SUBCHROWLE TOXICITY STRIDY IN RATS

PRINTED: 12-MAY-88 PAGF: 288

STUDY NIMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: B08501 SEX: MALE DATE OF DEATH: 07/16/86 STUDY DAY OF DATE AND TIME OF NECROPSY: 07/16/86 13:47 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL	DEATH	DOSE GROUP: 4 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE 1975 STUDY WEEK NF DEATH: 14 TERMINAL BROY WEIGHT: 428.8 GRAMS PROSECTOR: DOUGLAS HERNDON RECORDER: SID JONES, DUM, PHD, I PATHOLOGIST: SID JONES, DUM, PHD, DACUP WEIGHFR: DOUGLAS HERNDON	SCHE 1ERM	DULED, TERMINAL SACRIFICE THAL ROOY WEIGHT: 428.0 GRAMS RECORDER: SID JONES, DUM, PHO, DAISUP WEIGHER: DOING AS HERNDON
ORGAN NAME	I ME I	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN IN BRAIN WEIGHT RATIO	ORGAN STATUS
ADRENAL (AD) BRAIN W/SIEM (BR) HEART (HT) SPLEEN (SP) KIDNEY (KD) LIUGR (LI) TESTIS/EPIDID (TP)	2.09 2.09 1.34 .65 3.41 13.29 5.86	.0146 % .489 % .312 % .152 % .796 % 3.115 %	. 0300 1.010 . 639 . 310 1.630 6.356	WEIGHT TAKEN LIETGHT TAKEN
CLINICAL OBSERVATIONS	P A T	O G Y O B S E R V A T NECROPSY	5 N O 1	H1STnfraTufa, nGY
-APPEARED NORMAL	GENERAL INFO	NERAL INFORMATION (XX);	LING CLU): -PERIBRONCHIAL/PERIUA INFILIRATION, LYMPHO MAMMARY GLAND (MS): >SECTION EXAMINED; TI PARATHYROID (PT): >SECTION EXAMINED; TI URINARY BLADDER (UB): >TISSUE MISSING	THE CLUD: - PERIBBRONCHIAL/PERIUASCULAR, - INFILITRATION, LYMPHOLD; - SLIGHT - SECTION EXAMINED; TISSUE NOT PRESENT - SINARY BLADDER (UB): - TISSUE MISSING

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/TOX SYSTEM FUITFUIT *** APPENDIX B

PRINTED: 12-MAY-80 PAGE: 281

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

RECORDER: SID JONES, DUM, PHD, DACUP 428.0 GRAMS SACRIFICE STATUS: SCHEDULFD, TERMINAL SACRIFICE METGHER: DOMES, AS HERNDON TERMINAL BINDY METGHT: PATHOLOGIST: SID JONES, DUM, PHD, DACUP STUDY WEEK OF DEATH: 14 PROSECTOR: DOUGLAS HERNOON DOSE GROUP: 4 STUDY DAY OF DEATH: 97 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL DATE AND TIME OF NECROPSY: 07/16/86 13:47 SEX: MALE DATE OF DEATH: 07/16/86 ANIMAL NUMBER: B08501

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (CA), THORACIC (AD), BORNE, FEMIR (FE), RORE, STFRRUM (SR),
BRAIN WASTEM (AR), CECUM (CD), CORO, CERVICAL (CS), CORO, LUMBAR (LC), CORO, THORACIC (TC),
BRAIN WASTEM (BR), CECUM (CD), COLON (CD), ESPURIT (CO), LORD, LUMBAR (LC), DECUMINAL (CE), KIDNEY (KD),
LACRIMAL GL, EXO (EO), LIVER (L), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MS),
MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MISCLE, SKELETAL (SM), NERUE, SCIATIC (SN), PARICREAS (FA),
PARATHYROID (PT), PITULITARY (PI), PROSTATE (PR), RECTUM (RE), SEMINAL VESICLE (SV), SKIN (SK), SKIN, OTHER (SS),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONSL (SU), TESTIS (TE), THYMIS (TH), THYRIID (TY), TRACHEA (TR),
URINARY BLADDER (UB), ACOLLECTED/TAKEN (XW)

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRTA, THORACIC (AD), BINNE, FEMUR (FE), BIONE, STERNIM (SR),
BRAIN WASTEM (BR), CECUM (CE), COLON (CD), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), EPIDIDYMIS (EP), ESOPHAGIS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JF), KIONEY (KD),
LACRIMAL GL, EXO (EO), LIVER (LI), LN, MESENTERIC (MS), MAND SALIVARY GL (SG), MARROW, STERHIM (SF),
MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), PANCREAS (PA), PITUITARY (PI), PROSTATE (PR), RECTUM (RF),
SEMINAL VESICLE (SV), SKIN (SK), SPLEEN (SP), STOMACH, RL (ST), SIOMACH, NOWGE, (SH), TESTES (TE), THYMIS (TH), FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: THYROID (TY), TRACHEA (TR) 뿔

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WFRE SAVED ***

*** PATH/TOX SYSTEM OUTPUT *** SUBCHRONIC TOXICITY STUDY IN RATS

INDIVIDUAL ANIMAL SUMMARY REPORT

PRINTED: 12-MAY-88 PAISE: 282

STUDY NUMBER: 2399108

DULED, TERMINAL SACRIFICE INAL BROY WEIGHT: 278.5 GRAMS RECORDER: SID JONES, DUM, PHD, DAEUP WEIGHER: BARBARA DAY	ORGAN STATUS	0248	
SCHE	ORGAN TO BRAIN METGHT RATIO	1.016 1.010 1.010 1.010 1.010 1.025 1.027 1.027 1.027 1.027 1.027 1.027 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037 1.037	1 1 1 1
WEEK O ARA DAY D JONES	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	. 0395 % . 0395 % . 244 % . 187 % . 596 % 2.395 % O B S E R U A T J NECROPSY ON (XX): OBSERUATIONS: NONE	1 1 1 1 1 1
. БЕАТН	ABSOLUTE ORGAN WEIGHT (GRAMS)	.050 .110 2.02 .68 .52 1.66 6.67 P A T H O L O G Y GENERAL INFORMATII	1 1 1 1 1 1 1 1 1
ANIMAL NUMBER: B08382 SEX: FEMALE DATE OF DEATH: 07/14/86 STUDY DAY OF DATE AND TIME OF NECROPSY: 07/14/86 9:21 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL	ORGAN NAME	ADRENAL (AD) DUARY (DU) BRAIN W/STEM (BR) HEART (HT) SPLEEN (SP) KIDNEY (KD) LIUGR (LI) CLINICAL OBSERUATIONS -APPEARED NORMAL	1 1 1 1 1 1 1

APPENDIX 8 *** PATH/IDX SYSTEM DUTPUT *** SUBCHRONIC TOXICITY STUDY IN RAIS

PRINTED: 12-MAY-88 PACE: 283

STRIDY NUMBER: 2399188

INDIVIDUAL ANIMAL SIMMARY REPORT

RECORDER: SID JONES, DUM, PHD, DACUP 278.5 GRAMS SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE WEIGHER: BARBARA DAY TERMINAL BRIDY WEIGHT: PATHOLOGIST: SID JONES, DUM, PHO, DACUP STUDY WEEK OF DEATH: 14 PROSECTUR: BARBARA DAY DOSE GROUP: 1 STUDY DAY OF DEATH: 95 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL 9:21 SEX: FEMALE DATE AND TIME OF NECROPSY: 07/14/86 DATE OF DEATH: 07/14/86 ANIMAL NUMBER: 808382

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ANRIA, THORACIC (AD), BINE, FEMIR (FE), BINE, STERNIM (SE),

BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),

BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), KIDNEY (KD), LASPRIMAL RI, FXXI (FD),

LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY (CS),

MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), NOARY (NU), PANCREAS (PA), PARATHYROID (FI),

PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, (XW)

THYMUS (TH), THYROID (TY), TRACHEA (TR), ERINARY BLADDER (LR), LIFRIS (HI), ACOURTED/TAKEN (XW)

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRIA, THORACIC (AD), BORE, FEMIR (FE), BONE, STERNIM (SB),
ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRIA (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
BRAIN WASTEM (BR), CECUM (CO), CORD, CORD, CERUICAL (CS), CORD, LAMBAR (GD), LIDER (LI),
LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROM, STERNUM (SE), MISCLE, SKELETAL (SM),
NERUE, SCIATIC (SN), OUARY (OU), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), KECTIM (RE), SKIN (SK),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BIADDER (UB) FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: 뿔

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAUED ***

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/TOX SYSTEM NITPUT *** APPENDIX B

PRINTED: 12-MAY-80

INDIVIDUAL ANIMAL SUMMARY REPORT

STEEP NIMBER: 239918

SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE TERMINAL BODY WEIGHT: PATHOLOGIST: SID JONES, DUM, PHD, DACUP STUDY WEEK OF DEATH: 14 PROSECTOR: TIM GROUE DOSE GROUP: 1 DEATH: 95 STUDY DAY OF POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL DATE AND TIME OF NECROPSY: 07/14/86 10:21 DATE OF DEATH: 07/14/86 ANIMAL NUMBER: B08383

RECORDERS SID JOHES, DUM, PHD, DACUP 247.1 GRAMS

WEIGHER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO DRGAN WEIGHTS RECORDED ***

CLINICAL OBSERVATIONS -APPEARED NORMAL -GLOBE RUPTURED POST MORTEM; RIGHT -GLOBE RUPTURED ROST MORTEM; RIGHT -GLOBE RUPTURED POST MORTEM; RIGHT -GLOBE RUPTURED RUPTURED POST MORTEM; RIGHT -GLOBE RUPTURED

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AD), BONE, FEMINE (FE), BUNE, STERNIM (SB),
BRAIN WASTEM (BR), CECUM (CE), COLON (CD), CORO, CFRUICAL (CS), CHRD, LIMBAR (LC), CHRD, THORACIC (TC),
DUDDENIM (DU), ESCHHAGUS (ES), HEART (HT), ILEUM (IL), JEDUNUM (JE), KIDNEY (KD), LACRIMAL GI, EXO (FO), LIVER (LT),
LN, MESENTERIC (MS), LN, OTHER (LN), LING (LU), MAMMARY GLAND (MS), MAND SALIVARY GI (SG), MARRIMA (SF),
MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), DUARY (DU), PANCREAS (PA), PARATHYROID (PT), PITULTARY (PI), RECTIM (RF),
SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), SIOMACH, NERGE (SD), THYRUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT) THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRIA, THORACIC (AN), BUNE, FEMUR (FE), BUNE, STERNIM (SB),
BRAIN WASTEM (BR), CECLM (CE), COLON (CD), CORD, FERUICAL (CS), CORD, LIMBAR (FD), THINACIC (TC),
BUDDENUM (DU), ESOPHABUS (ES), HEART (HT), ILEUM (IL), JEINNUM (JE), KIDNEY (KD), LACRIMAL GI, EXO (ED), LIOFR (LD),
LN, MESENTERIC (MS), MAMMARY GLAND (MS), MAND SALIVARY GL (SG), MARKHIM, STERUM (SF), MISCOF, SKEPETON (SM),
NERUE, SCIATIC (SN), DUARY (DU), PANCREAS (PA), RECTUM (RE), SKIN (SK), SPLEEN (SP), STOMACH, GI (ST),
STOMACH, NONGL (SU), THYMUS (TH), THYROID (TY), TRACHEA (TR), HRINARY BLADDER (LB), HIFRES (HT) FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: 뿔

APPENDIX 8 *** PATH/TOX SYSTEM DUTPUT *** SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88 PAGE: 285

STUDY NUMBER: 2597188

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: 808784 SEX: FEMALE DATE OF DEATH: 07/14/86 STUDY DAY 01 DATE AND TIME OF NECROPSY: 07/14/86 12:57	F DEATHS	DUSE GROUP: 1 SACRIFICE STAT : 95 STUDY WEEK OF DEATH: 14 PRISECTIOR: BARBARA DAY	SCHE	DULED, TERMINAL SACRIFICE INAL BODY WFIGHT: 297.1 GRAMS * RECORDER: SID JONES, DUM, PHD, DACUP	i .
POST-FIX WEIGHER: NOT REGUIRED BY PROTOCOL	1	PATHOLOGIST: SID JONES, DUM, PHD, DACUP	ACUP WEIGHER: BARBARA DAY	квака оау	- ;
ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO RODY WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO	ORGAN STATUS	
ODDEHOI (OD)	1 480	. 0281	. 11414	LIFT THREN	
COMPAN (COM)	850	.0196 %	,0289	METGHT TAKEN	
BRAIN WASTEM (BR)	2.02	% 629°	1.010	WFIGHT TAKEN	
	.85	.288 %	.423		
	. 58	% 961°	.288	LFIGHT TAKEN	
	1,79	.604 %	.839	WEIGHT TAKEN	
_	6.58	2.216 %	3.263	METCHT TAKEN	
		NULTEURSEU Y SO	NS	, , , , , , , , , , , , , , , , , , , ,	i .
CLINICAL OBSERVATIONS		<u>u</u>		HISTOPATHOLOGY	
RIGHT EYE-CHROMODACRYORRHEA;	GENERAL INFORMAT NOTE;>EXTERNA OBSERVA FYE-CHRI	GENERAL INFORMATION (XX): >MOTE:>EXTERNAL OBSERVATIONS:MALDCCLUSION, RIGHT EYE-CHRIMODACRY(IRRIIFA	1	LUNG (L.D.): -PERTERPREDION, I YMPHOLD,-SLIGHT INFILITRATION, I YMPHOLD,-SLIGHT flucky (flu): -LINILATERALLY EXAMINED,-PRESENT PITHITARY (PL): -CYST,-PRESENT	İ

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/TOX SYSTEM DUITFUIT ***

PRINTED: 12-MAY-88

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

SACRIFICE STATUS: SCHEDULFD, TERMINAL SACRIFICE	LEMBINAL BOUNT WEIGHT: 297.1 SWARDS RECTROFR: SID INNES, DUM, PHD, DACUP	į
ì	SIUDY WEEK UF DEAIM: 14 RARBARA DAY	PATHOLOGIST: SID JONES, DUM, PHD, DACUP
	DEATH: 99 PROSECTOR:	DL PATHOLOGIST: SI
SEX: FEMALE	S1U0Y DAY L 3Y: 07/14/86 12:57	COUIRED BY PROTOCO
ANIMAL NUMBER: B08384	DATE OF DEALM: U//14/86 STUDY DAY UP OATE AND TIME OF NECROPSY: 07/14/86 12:57	POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AR), ADRIA, THORACIC (AD), BITHE, FEMIRE (FE), BITHE, STERNIM (SR), BRAIN WASTEM (BR), CECUM (CE), COLON (CD), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TD), DUDDENUM (DU), ESOPHAGUS (ES), EYE (EY), HFART (HT), ILEUM (LL), ASINIMIN (JE), KIDHEY (LD), LACRIMAR (E, EXD (FD), MAND SALIVARY (CR), LACRIMAR (LD), MAND SALIVARY (CR), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), DUARY (DU), PANCREAS (FA), PARAHYROLD (FT), PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONIGL (SI), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (LH), HTERIS (LT), ACHIECTED/TAKEN (XW)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ANRIA, THORACIC (AD), BONE, FFMIR (FE), BONEAL, CORTEX (AC), COLON (CD), CORD, CORD, CONTO, CORD, THORACIC (TC), BRAIN WASTEM (BR), CECUM (CE), COLON (CD), CORD, CONTO, CONTO STOMACH, NONGL (SU), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UR), UTERUS (UT)

*** ALL ORGANS/TISSIES (REQUIRED TO BE HARVESTED PER THE STIMY PROTOCOL) LIFEE SAMED ***

A** PATH/TOX SYSTEM GUIPHT *** SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88 PAGE: 287

STHDY NUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: 808785 SEX: FEMALE DATE OF DEATH: 07/14/86 STUDY DAY OF DATE AND TIME OF NECROPSY: 07/14/86 13:40 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL	DEATH	WEEK O LAS HER D JONES	SCHF TERM	SCHEDNIED, TERMINAL SACRIFICE TERMINAL BROY WEIGHT: 262.4 GRAMS RECORDER: SID JONES, DUM, PHD, DACUP WEIGHER: DOUGLAS HERNOON
ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN WEJEHT RATIO	STATE
ADREMAL (AD)	. 058	20 0 5 5 0 C C C C C C C C C C C C C C C	2620.	WEIGHT TAKEN
DUARY (DU) ARAIN WASTEM (AR)	1.97	, 05/6 % 25/7,	1.000	METCHT TAKEN
HEART (HT)	1.05	% 66£°	.530	
SPLEEN (SP)	.41	.157 %	.249	LIF JCHT TOKEN
	2.00	.761 %	1.012	WEIGHT TAKEN
LIVER (LI)	7.07	2.696 %	3,685	UFICHT TAKEN
CLINICAL OBSERVATIONS	r G	HOLOGY OBSERUATION NECROPSY	s z	HISTOPATHOLOGY
-APPEARED NORMAL	UTERUS (UT) -LUMEN, FLUI GENERAL INFORM	UTERUS (UT): -LLMEN, FLUID; BOTH HORKS, CLEAR GENERAL INFORMATION (XX): >MOTE:>EXTERNAL OBSFRUATIONS:NOWF	LUNG (LID : -PERIBRAMUMIAL/PERIUAL INFILTRATION, LYMPHD UTFRUS (UT) : -DILATATION,-MUDERATE	NG (LID): -PERIBRATAHAL/PERIVASCULAR, INFILTRATION, LYMPHOID,-SLIGHT FRUS (UI): -DILATATION,-MODERATE

APPENDIX 8 *** PATH/TOX SYSTEM DIITPLIT *** SUBCHRONIC TOXICITY STUDY IN RATS

PRINTFU: 12-MAY-RS PACE: 288

STUDY MIMBER: 2399108

INDIVIDIAL ANIMAL SHMMARY REPORT

HINAL BODY WEIGHT: 262.4 GRAMS RECTROFER STD JONES, DUM, PHD, DACUP SACRIFICE STATUST SCHEDULED, TERMINAL SACRIFICE WEIGHER: DOUGLAS HERNDON TERMINAL BODY WEIGHT: PATHOLOGIST: SID JONES, DUM, PHD, DAILUP STUDY WEEK OF DEATH: 14 PROSECTOR: DOUGLAS HERMININ DOSE GRITCIP: 1 STUDY DAY OF DEATH: 95 POST-FIX WEIGHER: NOT REGUIRED BY PROTOCOL SEX: FEMALE AND TIME OF NECROPSY: 07/14/86 13:40 DATE OF DEATH: 07/14/86 ANIMAL NUMBER: B08385

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AD), RINE, FEMIR (FE), BOWE, STERNIM (SB),
BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HI), ILEMM (11), DEDUNIM CA), KIDNEY (KO), LACRIMAL SI, EXC (FD),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MS), MAND SALIVARY GL (SG),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERUE, SCIATIC (SN), CHARY (RU), PANTKEAS (PA), PARATHYROLD (FT),
PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN (SK), BLADDER (LB), ADOLE (SP), STOMACH, GL (ST), STOMACH, NINGL (SL),
THYMUS (TH), THYROLD (TY), TRACHEA (TR), HRINARY BLADDER (LB), ADOLE (SD), ADOLE (KA) THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AURTA, THORACIC (AD), BUNE, FEMUR (FE), BONE, SIFRNUM (SH),
BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORO, CERVICAL (CS), CORD, LUMBAR (LC), CORO, THORACIC (TC),
DUDDENUM (DU), ESOPHAGUS (ES), FYE (EY), HEART (HT), ILFUM (IL), LEMINIM (LF), KIDNEY (KD), LACRUMAL R., EXO (FU),
LIVER (LI), LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIDARY GL (SR), MARROW, STERNUM (SE), MUSCLE, SKFLETAL,
NERUE, SCIATIC (SN), DUARY (DU), PANCREAS (PA), PARATHYROLD (FT), PITHITARY (PI), RECTUM (RF), SKIN (SK),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), THYMUS (TH), THYROLD (TY), TRACHEA (TR), URINARY BLADDER (IB) FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

A** PATH/TIN SYSTEM DITPIT *** SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88 PAGE: 289

STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL SHMMARY REPORT

TERMINAL BODY WEIGHT: 243.6 GRAMS RECORDER: SID JOHES, DUM, PHD, DACUP WETGHER: NOT REQUIRED BY PROTOCOL 243.6 GRAMS SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE PATHOLOGIST: SIO JONES, DUM, PHO, DACUP STUDY WEEK OF DEATH: 14 PROSECTOR: DOUGLAS HERNOTIN DOSE GROUP: 1 STUDY DAY OF DEATH: 96 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL SEX: FEMALE 9:19 DATE AND TIME OF NECROPSY: 07/15/86 DATE OF DEATH: 07/15/86 ANIMAL NUMBER: BOB386

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

-FOLL OF MONOBURY, FAR CELLS, -MINIMAL INFILTRATION, LYMPHOLO, -SLIGHT -PERIBRONICHIAL/PERIUASCIII AR, HISTOPATHOLOGY VINREMARKER E : (17) LIVER PATHOLOGY OBSERVATIONS -PALE AREA; BOTH, SEVERAL, TAN, 1 X 1 *COLLECTED/IAKEN (XM) : -ELECTRON MICROSCOPY SAMPLE; LIUER >NOTE:>EXTERNAL OBSERVATIONS:NONE GENERAL INFORMATION (XX) : NECROPSY .. (29) KIDNEY CLINICAL DBSERVATIONS -APPEARED NORMAL

ADRENAL, CORTEX (AC), ADRENAL, MEDILLA (AM), ADRIA, THORACIC (AC), BIRE, FFMIR (FF), FIRE, SIFREEM (EC),
BRAIN WYSTEM (BR), CECUM (CO), CORO, CORO, LUMBAR (LC), CORO, THORACIC (TC),
DUDDENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HI), ILEUM (II), JEJINEM (JF), (ATREMAL GI, FXO (EO), 1 JUFR (ID),
LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG), MAND SAI IVARY GL (SS), MARRIN, STERNUM (SF),
MUSCLE, SKELETAL (SM), NERUE, SCIATIC (SN), OVARY (DU), PANISEAS (PA), PARRIHYROID (PI), PITHITARY (PI), REFILM (KF),
SKIN (SK), SKIN, OTHER (SS), SPLEN (SP), STOMACH, GL (ST), STOMACH, NOWEL (SD), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT) THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AURTA, THORACIC (AD), BURE, FEMIR (FE), RIDE, STERRID (SB),
BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORO, CERUICAL (CS), CORO, LUMBAR (LC), CORO, THURACIC (TC),
DUDDENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (LL), JELINIM (JE), LACRIMAL A, FXO (FO),
LN, MESENTERIC (MS), MAMMARY GLAND (MS), MAND SALIVARY GL (SG), MARROW, STERNIM (SF), MUSCLE, SKFLEIAL (SM),
NERUE, SCIATIC (SN), DUARY (DU), PANCREAS (PA), PARATHYROD (FI), PICCITIARY (PI), RECTUM (RE), SKIN (SK),
SPLEEN (SP), STOMACH, GL (SI), STOMACH, NONSL (SU), THYMUS (TH), THYROD (TY), TRACHEA (TR), URINARY BLADDER (LB), FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: 里

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STIDY PROTUGUE) WHAE SAULD ***

APPENDIX 8 *** PATH/TOX SYSTEM DUTPUT *** SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 19-MAY-88 PAGE: 298

STUDY NUMBER: 9399118

INDIVIDUAL ANTMAL SUMMARY REPORT

ANIMAL NUMBER: B08387 SEX: FEMALE DATE OF DEATH: 07/14/86 STUDY DAY OF OATE AND TIME OF NECROPSY: 07/14/86 15:07 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL	. ОЕАТН	, WEEK C GROVE D JONES	SCHE	ONEED, TERMINAL SACRIFICE INAL BOOY WEIGHT: 257.0 GRAMS RECORDER: SID JONES, DOM, PHD, DATUP WEIGHER: IIM GRIVE
ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORSAN WEIGHT RELATIVE TO FIODY WEIGHT (%)	ORBAN TO BRAIN	2 4 5 4 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5
ADRENAL (AD) OUARY (OU) BRAIN W.STEM (BR) HEART (HT) SPLEEN (SP) KIDNEY (KD) LIUER (LI)	. 062 . 124 1.99 . 84 . 56 1.73 6.24			LETIGHT TRKEN LETIGHT TAKEN LETIGHT TAKEN LETIGHT TAKEN LETIGHT TAKEN LETIGHT TAKEN LETIGHT TAKEN
CLINICAL OBSERVATIONS		OBSERUAT	5	HESTOPATHOLOGY
-APPEARED NORMAL	GENERAL INFO	GENERAL INFORMATION (XX); >NOTE:>EXTERNAL TRISFRUATIONS:NONE	ADRENAL, CORTEX (AC): -DFAFFERATION, MINIMA EYE (EY): -CHROWIC HETAMATION SLIGHT -FOCI OF MONONLICLEAR LUNG (LU): -FOCI OF MONONLICLEAR LUNG (LU): -FOCI OF MONONLICLEAR	RENAL, CORTEX (AC): -DEATHERATION,-MINIMAL E (EY): -CHROLIC HIELAMMATION, HARDFRIAN GLAND,-SLIGHT VER (LI): -FOCI OF MONDAMICLEAR CELLS,-MINIMAL -PRINTMAHAMATION, LYMPHOID,-SLIGHT

APPENDIX 8 *** PATH/TOX SYSTEM GLITFILE *** SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-8R PAGE: 291

STRINY NEWERS 2399109

INDIVIDIAL ANTMAL SUMMARY REPURT

RECORDER: SID JONES, DUM, PHD, DACUP 257.0 GRAMS SADRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE TERMINAL BODY WEIGHT: WEIGHER: TIM GROUE PATHOLOGIST: SID JONES, DUM, PHO, DALUP STUDY WEEK OF DEATH: 14 PROSECTOR: TIM GROVE DOSE GROUP: 1 SEX: FEMALE DOS STUDY DAY OF DEATH: 95 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL DATE AND TIME OF NECROPSY: 07/14/86 15:07 DATE OF DEATH: 07/14/86 ANJMAL NUMBER: B08387

ABRENAL, CORTEX (AC), ADRENAL, MEDILLA (AM), ANRIA, THORACIC (AD), BONE, FEMIR (FF), BANE, SIFRING (GB),
BRAIN WASTEM (BR), CECUM (CE), COLON (CD), CORD, CERUICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
BUDDENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HI), ILEUM (IL), DETINING (DF), KIDMEY (KD), LATRINGL SI, EXD (FN),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MS), MAND SALIVARY G (SS),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERUE, SCIATIC (SN), OVARY (NO), PANCREAS (PA), PARATHYROID (PI),
PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, MINGL (SID),
THYMUS (TH), THYROID (TY), TRACHEA (TR), HRINARY BLADOFR (1R), HTFRIS (1D), COULECTED TAKE (XA) THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, MEDULLA (AM), ADRTA, THORACIC (AD), BUNE, FEMIR (FE), BUNE, STERNEM (SB), BRAIN WASTEM (FR), CECHM (CE), COLON (CO), CORO, CERUICAL (CS), CORD, LUMBAR (LC), CORO, THORACIC (TC), DUIDDENIM (DI), ESOPHABLE (ES), HEART (HT), LEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL BL, EXO (FO), IN, MESENTERIC (MS), MAMMARY GL (SC), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), QUARY (DU), PANCREAS (PA), PARATHYROID (PT), PITULIARY (PI), RECTUM (RE), SKIN (SK), SPLEEN (SP), STOMACH, GL (ST), STOMACH, HOWGL (SO), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT) THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

*** ALE ORGANS/IISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

*** PATH/TOX SYSTEM DITPUT *** SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88 PAGE: 299

INDIVIDUAL ANIMAL SHMMARY REPORT

STIDY NIMBER: 2399108

URIE AND 11ME UF NELKUPSY: U//14/46 15:13 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL	PRI	SECTIN: DIMINIAS HERMONN HOLOGIST: SID JONES, DUM, PHO, DACUP	- i	MEIGHER: DESIGNS HERNON
ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORSAN TO BRAIN METSHI RATIO	0 R G A N S T A T U S
ADREMAI (AD)	. 848	. 1192 %	. 0256	LEIGHT TAKEN
DUARY (DU)	0.60	% 63£0.	. 0479	WEIGHT TAKEN
BRAIN WASTEM (BR)	1.88	250 %	1.6110	. METCHT TAKEN
HEART (HT)	68.	.354 %	. 471	WELGHT TAKEN
SPLEEN (SP.)	49.	2000年 2000年	. 742	LIFTIGHT TAKEN
K (DNEY (KD)	1.68	× 299.	. 839	WEIGHT TAKEN
LIVER (LD	6.62	2.634 %	3.531	WEIGHT TAKEN
CLINICAL DASERVATIONS	PATHOL	HOLOGY OBSERUATIONS NECROPSY		HISTOPATHOLOGY
-APPEARED NORMAL	GENERAL INFORMA VIOLES SEXTERN	L INFORMATION (XX): E:>EXTERNAL OBSERVATIONS:NOBE	LUNG CLU) : - PFR] HRBHCH	NG (LD): -PFRIBERGHALZPFRIUASIALIAR, INFILITRATION, LYMPHOLD,-SLIGHT

APPENDIX 8 *** PATH/IOX SYSTEM OUTPUT *** SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-RE PAGE: 293

INDIVIDUAL ANIMAL SUMMARY REPORT

STIENY MIMBERS 2399168

TERMINAL BIDY MEIGHT: 251.2 GRAMS RECORDER: SID JONES, DUM, PHD, DACUP SACRIFICE STATUS: SCHEDULFD, TERMINAL SACRIFICE WEIGHER: DOWNLAS HERNDON PATHOLOGIST: SID JONES, DUM, PHD, DACUP H: 95 STIJDY WEEK OF DEATH: 14 PROSECTOR: DOUGLAS HERNOTIN DOSE GROUP: 1 STUDY DAY OF DEATH: 95 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL DATE AND TIME OF NECROPSY: 07/14/86 15:13 SEX: FEMALE DATE OF DEATH: 07/14/86 ANIMAL NUMBER: B08388

ADRENAL, CORTEX (ACT), ADRENAL, MEDILLA (AM), ADRIA, THORAGIC (AD), BORE, FEMIR (FE), BORE, SIERHIM (SR),
BRAIN LOSTEM (BR), CECUM (CE), CORO, CORO, CERVICAL (CS), CORO, LUMBAR (LC), CORO, THORAGIC (TC),
BUODENUM (DU), ESDPHAGUS (ES), EYE (EY), HEART (HT), ILEIM (IL), JEDIRUM (DE), KIDNEY (KD), LACRIMAL GI, EXD (EU),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GI (SG),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERUE, SCIATIC (SN), NUARY (NU), PARTREAS (PA), PARATHYRIID (PT),
PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, MINISL (SID),
THYMUS (TH), THYROID (TY), TRACHEA (TR), IRINARY BLADDER (118), 11FRUS (117), ACOHECTED/TAKEN (XM) THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRIA, THURACIC (AD), PUNE, FFMIR (FE), PUNE, SIFRRUM (SB),

BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORO, CERUICAL (CS), CORO, LUMBAR (LC), CORO, THURACIC (TC),

DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), AEMINAM (AE), KIDAKY (KD), LACRIMM (SE), MISCLE, SKELETAL (SM)

LIVER (L1), LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SS), MARROW, STERNIM (SE), MISCLE, SKELETAL (SM),

NERUE, SCIATIC (SN), DUARY (DV), PANCREAS (PA), PARATHYROLD (TY), TRACHEA (TR), URINARY BLADDER (UR),

SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), THYMUS (TH), THYROLD (TY), TRACHEA (TR), URINARY BLADDER (UR), UTERUS (UT) 里

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOU) WENE SAUFD ***

SUBCHRONIC TOXICITY STRIDY IN RATS *** PATH/TOX SYSTEM BUTPUT *** APPENDIX 8

PRINTED: 12-MAY-88

INDIVIDUAL ANIMAL SUMMARY REPORT

PAGE 1 294

STUDY NUMBER: 2399108

SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE PATHOLDGIST: SID JONES, DUM, PHD, DACUP STILDY WEFK OF DEATH: 14 PROSECTOR: BARBARA DAY DOSE GROUP: 1 STUDY DAY OF DEATH: 96 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL DATE AND TIME OF NECROPSY: 07/15/86 10:44 DATE OF DEATH: 07/15/86 ANIMAL NUMBER: B08389

TERMINAL BROY METGHT: 267.0 GRAMS RECORDER: SID JONES, DOM, PHD, DACUP WETCHER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

CLINICAL OBSERVATIONS

-APPEARED NORMAL

PATHOLOGY OBSERUATIONS NECROPSY

-ELECTRON MICROSCOPY SAMPLE; I TUER >NOTE:>EXTERNAL DASERVATIONS:NONE GENERAL INFORMATION (XX) : COLLECTED/TAKEN (XW) :

SSECTION EXAMINED, TISSUE NOT PRESENT -FORT OF MONTHAND FAR CELLS, - MINIMAL INFILTRATION, LYMPHOTO, -SLIGHT - PERTHERMINENTAL ZPERTUASIBILIAR PARATHYROID (PT): LIVER (L.1) : CON CLUB

HISTOPATHOLOGY

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDILLA (AM), ANRIA, THORACIC (AN), BOHE, FFMIR (LF), BOHE, STERNIM (SB),
BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORD, CERUICAL (CS), CORD, LLMBAR (LC), CORD, THORACIC (TC),
DUDDENUM COU), ESOPHAGUS (ES), FYE (EY), HEART (HT), ILEUM (IL), AFJUNIM CAE), KIDNEY (KD), LACRIMAL NA, FXO (ED),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLANO (MS), MAND SALIVARY GL (SB),
MARROW, STERNUM (SE), MUSCLE, SKELFTAL (SM), NERVE, SCIATIC (SN), OWARY (OU), PANCREAS (PA), PARATHYROID (PT),
PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SID),
THYMUS (TH), THYROID (TY), TRACHEA (TR), INFINARY SLADGER (11B), HIFRIS (HF)

ADRENAL, CORTEX (AC), ADRENAL, MEDILLA (AM), AGRIA, THORACIC (AD), BRNE, FFMIR (FF), RINE, STERNIM (SA),
BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORO, CERVICAL (CS), CORO, LUMBAR (LC), CORO, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), FYE (EY), HEART (HT), ILEIM (HI), JENINAMM (JE), KIDHEY (KD), FANERIAS (H),
LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNIM (SE), MISCLE, SKELETAL (SM),
NERVE, SCIATIC (SN), CWARY (DU), PANCREAS (PA), PITHITARY (PI), RECHMA (RE), SKIH (SK), SHIFFH (SP),
STOMACH, GL (ST), STOMACH, NONGL (SU), THYMUS (TH), THYROID (TY), TRACHEA (TR), LIRINARY BLADDER (HR), UTERES (HI) THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/TOX SYSTEM CHUPHU *** 8 XION3dde

PRINTEDS 12-MAY-80 PAGF: 295

STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

-CHRONIC INFLAMMATION, HARDERIAN GLAND,-RECORDER: SID JONES, DUM, PHD, DACUP 261.7 GRAMS TAKEN TAKEN TEKEN WEIGHT TAKEN TAKEN METCHT TAKEN METGHT TAKEN 51818 2000 HISTOPATHOL DISY SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE ME JOHT LE I GHT ME I SHI **WEIGHT** WEIGHER: BARBARA DAY TERMINAL BOOK WEIGHT: EM: (£Y) : TO THE IN DRGAN TO BRAIN WEIGHT RATIO .0278 . 0925 330 906. 1.800 .391 3.572 PATHOLOGIST: SID JONES, DUM, PHD, DACUP 08SERUAT 10N STUDY WEEK OF DEATH: 14 >NOTE:>EXTERNAL DBSERVATIONS:NONE DRGAN WEIGHT RELATIVE TO HOLY METCHT (%) .0210 % % 6690° .296 .680 956. . 55N GENERAL INFORMATION (XX) : PROSECTOR: HARBARA DAY MECRUPSY DOSE GROUP: 1 PATHOLOGY ABSOLUTE ORGAN WEIGHT SEX: FEMALE DOS STUDY DAY OF DEATH: 96 (GRAMS) .183 . 055 1.78 1.98 . 65 7.07 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL DATE AND TIME OF NECROPSY: 07/15/86 8:45 CLINICAL OBSERUATIONS BRAIN W/STEM (BR) DATE OF DEATH: 07/15/86 ANIMAL NUMBER: B08390 (B) (SP) 9 9 (1) Œ ORGAN NAME -APPEARED NORMAL ADREMAL SPLEEN KIDNEY DUARY LIVER HEART

INFILTRATION, LYMPHOID, -SLIGHT

-PERIBRIMENIAL /PERIOASEM AR,

3

APPENDIX B *** PATH/TITX SYSTEM DITPLIT *** SUBCHRONIC TOXICITY STUDY IN RAIS

PRINTED: 12-NAY-8:: PAGE: 294

INDIVIDINE ANIMAL SUMMARY REPORT

STREET NUMBER: 2399188

RECORDER: SID ATHRES, DUM, PHD, DAILUP 261.7 GRAMS SACRIFICE STATUS: SCHEDNIED, TERMINAL SACRIFICE WEIGHER: BARBARA DAY TERMINAL BODY WEIGHT: PATHOLOGIST: SID JONES, DUM, PHD, DACUP STUDY WEEK OF DEATH: 14 PROSECTOR: RARBARA DAY DOSE GROUP: 1 STUDY DAY OF DEATH: 96 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL DATE AND TIME OF NECROPSY: 07/15/86 8:45 DATE OF DEATH: 07/15/86 ANIMAL NUMBER: B08390

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AFRIA, THORACIC (AD), BINE, FFMIR (FE), BONE, SIFRHUM (SB),
BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
BUDDENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEMM (IL), JECHNUM (DI), KIDNEY (KO), LATRIMAL SI, FXR (FD),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY G. (SR),
MARROW, STERNUM (SE), MUSCLE; SKELETAL (SM), NERUE, SCIATIC (SN), QUARY (RU), PANCREAS (PA), PARATHYRUD (PI),
PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN (SK), SKIN (SK), SKIN (SK), BLEEN (SP), STOMACH, G. (ST), STOMACH, NINGL (SU),
THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (18), LITERIS (LI), ~COLLECTED/TAKEN (XL) THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AGRIA, THORAGIC (AD), BONE, FFMIR (FF), BURE, SIFRNIM (SB),
BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORAGIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), HEART (HT), ILEUM (IL), JEJUNIM (JF), KIDNIY (KD), FACRIMAN (B), FXO (FD),
LN, MESENTERIC (MS), MAMMARY GLAND (MS), MAND SALIVARY (BL (SG), MARROLL, STERNIM (SE), MUSCLE, SKELETAL (SM),
NERVE, SCIATIC (SN), DUARY (DU), PANCREAS (PA), PARATHYROID (PT), PITHITARY (PI), RECTHM (RF), SKIN (SK),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (LR), FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: 뿔

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STIMY PROTOCOL) WERE SAULD ***

APPENDIX B *** PATH/IDX SYSTEM DUITPUL *** SUBCHRONIC TOXICITY STUDY IN RATS

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INDIVIDUAL ANIMAL SHMMARY REPORT

STIDY NUMBER: 2399108

ANIMAL NUMBER: B08391 SEX: FEMALE DATE OF DEATH: 07/15/86 STUDY DAY OF DATE AND TIME OF NECROPSY: 07/15/86 14:50 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL	. ВЕАТН	MEEK O	SCHE	OUR FD, TERMINAL SACRIFICE INAL BROY WEIGHT: 227.8 GRAMS RECKROFR: SID JOHES, DUM, PHD, DARVP WEIGHER: IIM GROVE
ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO RODY WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO	086AX STATUS
1 ~		.0382 x	. 0526 . 0576	LETCHT TAKEN WEIGHT TAKEN LETCHT TAKEN
BRAIN WASTEM (BR) HEART (HT) SPLEEN (SP) KIDNEY (KD) LIUER (LI)	1.84 .79 .51 1.74 7.47	. 262 % . 184 % . 626 % . 639 %	1,560 429 227 . 946 4,060	
CLINICAL OBSERVATIONS	_	HOLOGY OBSERVATIONS NECROPSY	8 N U	нтаторатносову
-APPEARED NORMAL	UTERUS (UT) -LIMEN, FLI GENERAL INFOI >NOTE:>EXT	UTERUS (UI): -LUMEN, FLUID; BOTH HURHS, CLEAR GENERAL INFORMATION (XX): >NOTE:>EXTERNAL DARERUATIONS:HOWE	LIVER (L.): -FRET OF MORTERERS LLING (L.): -PERTREMENTAL PERTURA INFLITERIS (1): -DILATATION, LYMPHO	UER (LI): -FOCI OF MONIBURGLEAR CELES,-MINIMAL NG (LE): -PERIBRUMCHIALZPERIVASCULAR, INFILITRATION, LYMPHOID,-SLIGHT FRUS (HI): -DILATATION,-MODERATE

A** PATH/INX SYSTEM DUTPUT *** SUBCHRONIC TOXICITY STUDY IN RATS

FRINIED: 12-MAY-80 PAGE: 298

STHDY NUMBER: 23991118

INDIVIDUAL ANIMAL SUMMARY REPURT

RECOMMENS STO JUNES, DUM, PHD, DACUP TERMINAL BRIDY LIFTGHTE - 227. R SRAMS SACRIFICE STATUS: SCHEDULFO, TERMINAL SACRIFICE WEIGHER: TIM GRIVE PATHOLOGIST: SID JOHES, DUM, PHD, DACUP STUDY WEFK OF DEATH! 14 PROSECTOR: TIM GROUF STUDY DAY OF DEATH: 96 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL DATE AND TIME OF NECROPSY: 07/15/86 14:50 DATE OF DEATH: 07/15/86 ANIMAL NUMBER: 808391

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRIA, THORACIC (AD), BORE, FFMIR (FF), BORE, SIFRWIM (SR), BRAIN WASTEM (BR), CECUM (CE), COLON (CD), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC), DUBDENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), HEUM (LL), ALMINEY (LD), KITMEY (LD), LAGRETIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARCLE, SKELETAL (SM), HENCE, SCIATIC (SN), NOARY (NU), PAHTREOS (PA), PARATHYRNID (PT), PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN (SK), SKIN (SK), SKIN (SK), HRINARY GL (SP), STOMACH, GL (ST), STOMACH, MINSIE (SH), THYMUS (TH),
THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDILLA (AM), ACRIA, THURACIC (AD), ELWRE, FEMIRE (FF), ROLE, STERNIM (SR),
BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORD, CERUICAL (CS), CORD, LUMBAR (LC), CORD, THURACIC (TD),
DUODENUM (DU), ESOPHAGUS (ES), EYE (FY), HEART (HT), ILEIM (TC), JEJINGHM (JC), KIDNEY (KD), LAERIMAL (AL), FXM (FM),
LN, MESENTERIC (MS), MANMARY GLAND (MS), MAND SALIVARY GL (SG), MARROLM, STERNIM (SE), MISCLE, SKELETAL (SM),
NERUE, SCIATIC (SN), DUARY (DU), PANCREAS (PA), PARATHYROID (PI), PITHITARY (FI), KECHIM (RE), SKIN (SK),
SPLEEN (SP), STOMACH, GL (SI), STOMACH, NONGL (SU), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (LB)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STIMY PROTOCOL) WERE SAVED ***

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/TOX SYSTEM OUTPUT *** APPENDIX B

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INDIVIDIDAL ANIMAL SUMMARY REPURT

STUDY MIMBER: 2399188

TERMINAL BODY MEIGHT: 294.7 GRAMS RECORDER: SID ADMES, DUM, PHD, DACUP SACRIFICE STATERS SCHEDULED, TERMINAL SACRIFICE PATHOLOGIST: SID JONES, DUM, PHD, DACUP STUDY WEEK OF DEATH: 14 PROSECTOR: BARBARA DAY DOSE GROUP: 1 STUDY DAY OF DEATH: 97 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL 9:27 DATE AND TIME OF NECROPSY: 07/16/86 DATE OF DEATH: 07/16/86 ANIMAL NUMBER: BUB 392

WEIGHER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

CLINICAL OBSERUATIONS

-APPEARED NORMAL

PATHOLOGY DBSERVATIONS NECROPISY

-ELECTRON MICROSCOPY SAMPLE; 1 10FR ~COLLECTED/TAKEN (XW) :

MOTE: FYTERNAL DRSERVATIONS: NOWE GENERAL INFORMATION (XX):

SECTION EXAMINED; TISSINF NOT PRESENT -FOCT OF MINIMUM EAR CELLS, -MINIMAL INFILTRATION, LYMPHOLO, -SLIGHT - PERTERTHEM ALZPERTUASIUM AR PARAIHYRDID (PI): LIVER CLD: LUMB CLUD :

HISTOPATHOLOGY

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADERNAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ACRIA, THORACIC (AD), BONE, FEMIR (FE), BONE, STERNIM (SB),
BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LIMBAR (LC), CORD, THORACIC (TC),
DUDDONIM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEDUNIM (JE), KIONEY (KO), LACRIMAL GL, EXH (ED),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAD, MAND SMI JUARY GLOS,
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERUE, SCIATIC (SN), DUARY (DU), PANCREAS (PA), PARATHYRHIO (PI),
PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN (SK), SKIN (SK), SKIN (SK), LINGARY BLADDER (UR), UTERUS (UT)

FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCIPIC EXAMINATION: 뿔

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRIA, THORACIC (AD), BINE, FEMUR (FE), BINE, STERNUM (SR),
BRAIN WASTEM (BR), CECUM (CE), COLON (CD), CHRD, CERUTCAL (CS), CHRD, LHEBAR (LC), CARO, THARABLIC (TD),
DUGDENUM (DJ), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAR (B., EXI (FI),
LN, MESENTERIC (MS), MANMARY GLAND (MG), MAND SALIUARY (FI), MARRIAL, STERNIM (SF), MISCO F, SKILL (SN),
NERUE, SCIATIC (SN), DUARY (DU), PANCREAS (PA), PITUITARY (PI), RECTUM (RE), SKIN (SK), SPLEEN (SP),
STOMACH, GL (ST), STOMACH, NONGL (SU), THYMUS (TH), THYRUD (1Y), TRACHEA (TR), HIRTREY HEADER (1B), HIFRET (HT)

*** ALL DRGANS/TISSHES (REQUIRED TO BE HARVESTED FER THE STUDY PROTOCOL) WHEE SAUED ***

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/TRX SYSTEM DUTPLIT *** APPENDIX B

PRINTFD: 12-MAY-80 PAGE: 700

INDIVIDUAL ANIMA SUMMARY REPUBL

STUDY NUMBER: 2399108

WEIGHER: NOT REQUIRED BY PROTOCOL SACRIFICE STATUS: SCHEDULED, TECHNIAL SACRIFICE TERMINAL BODY WEIGHT: PATHOLOGIST: SID JONES, DUM, PHD, DACUP STIJDY WEEK OF DEATH: 14 PROSECTOR: DOUGLAS HERMOIN DOSE GROUP: 1 STUDY DAY OF DEATH: 97 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL DATE AND TIME OF NECROPSY: 07/16/86 10:35 SEX: FEMALE DATE OF DEATH: 07/16/86 ANIMAL NUMBER: B08393

RECORDER: SID JOHES, OUM, PHD, DACUP 266.0 GRAMS

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

HISTOPATHOLOGY LIVER (LI) : FUND CLED PATHOLOGY OBSERVATIONS COLLECTEDZTAKEN (XM) : -ELECTRON MICROSCOPY SAMPLE; LIUER MOTE: FXTERMAL DBSERVATIONS: NOWE GENERAL INFORMATION (XX): NECROPSY CLINICAL OBSERVATIONS -APPEARED NORMAL

-FREEL RIFFERENCE FAR CFILS, -MINIMAL INFILTRATION, LYMPHOID, -SI IGHT PERTURBATION APPRICABILITY OF PARATHYROID (PT):

SSECTION EXAMINED, TISSUE NOT PRESENT THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:
ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AURIA, THORACTE (AC), BUNE, FFMIR (FE), BUNE, STERNIM (SB),

BRAIN WYSTEM (BR), CÉCUM (CE), COLON (CO), CORO, CERVICAL (CS), CORO, LUMBAR (LC), CORO, THORACIC (TC), DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), LIEUM (LL), DELIBBUM (DE), KIDNÉY (KD), LADRIMAL RL, FYR (FD), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GI (SR), MARROW, STERNUM (SE), MISCLE, SKELETAL (SM), NFRUE, SCIATIC (SN), MUARY (MU), PANCREAS (PA), PARCHID (FT), PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPIEEN (SP), STOMACH, GL (ST), STOMACH, NGWGI (SH), THYMUS (TH), THYROID (TY), TRACHER (TR), HRIMARY BLADDER (MB), WIFRUS (MI)

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AURTA, THURACIC (AC), LUMBAR (LC), EDRO, THURACIC (TC), BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORO, CERUICAL (CS), CORO, LUMBAR (LC), CORO, THURACIC (TC), DUODENUM COU), ESOPHAGUS (ES), EYE (EY), HEART (HI), ILFIM (II), JOINING (JE), KIBBYY (CO), LATRIMAR GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SF), MESCLE, SKFLETAL (SM), NERUE, SCIATIC (SN), DUARY (GU), PANCREAS (PA), PITHITARY (FI), RECTIM (SE), SALETA (SP), SALETAL (SN), STOMACH, GL (SI), STOMACH, GL (SI), URINARY GLAD, THYROLD (TY), TRACHEA (TR), URINARY GLAD, DIFFRED (III) THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

APPENDIX B *** PATH/TOX SYSTEM OUTPUT *** SUBCHROUIC TOXICITY STUDY IN RAIS

PRINTED: 19-MAY-RB PAGE: 301

STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: B08394 SEX: FEMALE DATE OF DEATH: 07/15/86 STUDY DAY OF DFATH: DATE AND TIME OF NECROPSY: 07/15/86 13:51 PF POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL PY	SEX: FEMALE DOSE GR STUDY DAY OF DFATH: 96 715/96 13:51 PROSECTOR D BY PROTOCOL PATHOLOGI	DOSE GROUP: 1 SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE 1996 STUDY WEFK OF DEATH: 14 TERMINAL HODY WEIGHT: 942.5 GRAMS PROSECTOR: DOUGLAS HERNDON PATHOLOGIST: SID JOHFS, DUM, PHD, DAGUP WEIGHER: DOUGLAS HERNDON	SCHE	MEDULED, TERMINAL SACRIFICE RMINAL HIDY WEIGHT: 242.5 GRAMS RECORDER: 510 JONES, DUM, PHO, DACUP WEIGHER: DOMES AS HERNOTH
ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATION TO BODY WEIGHT (\$)	ORGAN TO ARAIN WEIGHT RATIO	DREAN STATHS
ADRENAL (AD) GUARY (DU) BRAIN W/STEM (BR) HEART (HT) SPLEEN (SP) KIDNEY (KD) LIVER (LI) CLINICAL OBSERVATIONS -APPEARED NORMAL	2.16 2.16 88 .88 .52 1.92 7.15 P	75 .0311 % 36 .0560 % 6 .890 % 890 % 2 .214 % .214 % .291 % 2 .948 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891 % 5 .891	1,000 1,000 408 241 889 3,315 1 0 N S HISTE 1 USE (1 1) : -FOCI OF MCHONIE'S LIBG (11) : -PRETERPONCHIAL /PE INTILERATION, L') -PNETERBINITIS, -SLI -PNETERBINITIS, -SLI -PNETERBINITIS, -SLI	0349 METGHT TAKEN 000 METGHT TAKEN 000 METGHT TAKEN 000 METGHT TAKEN 241 METGHT TAKEN 1241 METGHT TAKEN 1889 METGHT TAKE
			SECTION EXA	SECTION EXAMINED; TISSUF NOT PRESENT

APPENDIX 8 *** PAIH/10X SYSTEM DETPHIT *** SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88

INDIVIDUAL ANIMAL SUMMARY REPORT

STIEV HEMBER: 0799188

ANIMAL NUMBER: B08394	SEX: FEMALE	DOSE GROUP: 1	SACRIFICE STATUS	SACRIFICE STATUS: SCHFDUIFD, TERMINAL SACRIFICE
DATE OF DEATH: 07/15/86	STUDY DAY OF	DEATH: 96 STUDY WEI	STUDY WEEK OF DEATH: 14	TERMINAL BRIDY LIETGHT: 242.5 GRAMS
DATE AND TIME OF NECROPSY: 07/15/86 13:51	07/15/86 13:51	PROSECTOR: DOUGLAS HERNDON	HERNDIN	RECORDER: SID JONES, DUM, PHD, DAS
POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL	IRED BY PROTOCOL	PATHOLOGIST: SID JI	PATHOLOGIST: SID JONES, DUM, PHID, DAI:UP	WETGHER: DONGLAS HERNDON

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADREMAL, MEDULLA (AM), AORTA, THORACIC (AD), BIRLE, FEMIR (FE), BIRLE, STERNIM (SR),
BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
BUGDENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEIM (TL), DELIBNIM (LE), KIDHEY (KD), LACRIMAH (S., FXI (FID),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MS), MAND SALIVARY GL (SG),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERUE, SCIATIC (SN), NOARY (NU), PANCREAS (FA), PARATHYROID (PT),
PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), SIOMACH, NONGL (SID),
THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (NB), NIFRUS (NT), ^COLLECTED/TAKEN (XM)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACTIC (AD), BORD, LUMBAR (LC), CORD, THORACTIC (TC),
BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACTIC (TC),
DUDDENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), HEART (HT), AFTHAIN (AF), KIDNEY (KD), LACRIMAL (AL),
LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SC), MARROW, STERNUM (SF), MISCLE, SKELETAL (SM),
NERUE, SCIATIC (SN), DUARY (DU), PANCREAS (PA), PITUITARY (PI), RECTIMA (RE), SKIN (SK), SELFEN (SP),
STOMACH, GL (ST), STOMACH, NONGL (SU), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STLIDY PROTOCOL) WERE SAVED ***

APPENDIX 8 *** PATH/TOX SYSTEM DIDDIT *** SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88 PAISE: 303

STHIP MERRY 2399188

INDIVIDUAL ANTHAL SHMMARY REPRIRT

DIBED, TERMINAL SACRIFICE INAL BODY WEIGHT: 269.5 GRAMS RECORDER: SID JUNES, OUM, PHD, DACUP WEIGHER: BARBARA DAY	ORGANSIATUS	MFIGHT TOKEN MFIGHT TOKEN MFIGHT TOKEN		METCHT TAKEN WETCHT TAKEN	H1STOPATHOLOGY	UER (LI): -FICT OF MONOMETERR CELES,-MINIMAL NG (LD): -PERBORATHALZERIORSCHAR, INFILTRATION, LYMPHOLO,-SLIGHT -PREDMONITES,-MINIMAL
SCHE	ORGAN TO BRAIN MFIGHT RATIO	.0660	.388	1.033		LIVER (LI) : -FRCI OF NO LUNG (LI) : -PERISCIPATE INFILITMENT : -PRESIMONITEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCIPATEPERISCI
MEEK O	ORGAN WETGHT RELATIVE TO HODY WE HAHT (%)	. 0512 % . 0512 % . 0512 %	. 301 % . 197 %	,801 % 4,382 %	G Y O B S E R U A 1 NECROPSY	GENERAL INFORMATION (XX): >HOTE:>FXTERNAL OBSFROATIONS:HOUF
F DEATH	ABSOLUTE ORGAN WEIGHT (GRAMS)	191.	. 81 . 83	2.16	- v d	GENERAL INFOR
ANIMAL NUMBER: B08395 SEX: FEMALE DATE OF OEATH: 02/15/86 STUDY DAY OF DATE AND TIME OF NECROPSY: 02/15/86 14:36 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL	ORGAN NAME		BRHIN WASTER (BR) HEART (HT) SPIFFN (SP)	KIDNEY (KD)	CLINICAL OBSERVATIONS	APPEARED NORMAL

APPENDIX B *** PATH/IDX SYSTEM CHITPUT *** SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88 PAGE: 384

INDIVIDUAL ANIMAL SUMMARY REPORT

STHDY NUMBER 239910B

RECEIRDER: SED JOHES, DUM, PHD, DREWP 249.5 GRAMS SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE WFIGHER: BARBARA DAY TERMINAL BINDY LIFTIGHT: PATHOLOGIST: SID JONES, DUM, PHD, DACUP STUDY WEEK OF DEATH: 14 PROSECTOR: RARBARA DAY DOSE GROUP: 1 STUDY DAY OF DEATH: 96 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL SEX: FEMALE DATE AND TIME OF NECROPSY: 07/15/86 14:36 DATE OF DEATH: 07/15/86 ANIMAL NUMBER: 808395

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AIRTA, THORACIC (AD), BONE, FFMIR (FE), BONE, STERNIM (SB),
BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORO, CERUICAL (CS), CORO, LUMBAR (LC), CORO, THORACIC (TC),
DUDODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (LL), JEJINIM (JE), KIONEY (KD), LAFRIMAL GI, EXO (FD),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GI (SI),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERUE, SCIATIC (SN), FUNARY (DU), PANCREAS (PA), PARATHYROID (FI),
PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN (SK), BLADDER (1B), ITFRIS (HI), ATHIECT (SI), STOMACH, MINGL (SH),
THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (1B), HTFRIS (HI), ATHIECTEM (XM) THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDILLA (AM), ANRIA, THARACIC (AD), BIBLE, FFMIR (FF), BIBLE, STERNIM (SR),
BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORD, DERVICAL (CS), CORD, LUMBAR (LC), CORD, THARACIC (TC),
DUDDENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEIM (HI), JEDINUM (JE), KIDNEY (KD), LACRIMAL GL, FXO (FI),
LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROUL, STERNUM (SF), MUSCLE, SKELETAL (SM),
NERUE, SCIATIC (SN), DUARY (DU), PANCREAS (PA), PARATHYROID (PT), PITITIARY (PT), RECTUM (RE), SKIN (SK),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SD), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (LR), FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: 뿔

*** ALL ORGANSZIJSSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

APPENDIX'8 *** PATH/TOX SYSTEM OUTPUT *** SUBCHRINIC TOXICITY STUDY IN RAIS

PRINTED: 12-MAY-RB PAGE: 305

STIIDY NUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: B08396 SEX: FEMALE DATE OF DEATH: 07/15/86 STUDY DAY OF DEATH: DATE AND TIME OF NECROPSY: 07/15/86 15:11 PR POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL	SEX: FEMALE DOSE GROUP: 1 STUDY DAY OF DEATH: 96 STUDY 15/86 15:11 PROSECTOR: DOUG BY PROTOCOL PATHOLOGIST: SI	LAS HER D. Jrines	SCHE	SCHEDULED, TERMINAL SACRIFICE TERMINAL REDY WEIGHT: 248.6 GRAMS RECORDER: SID JONES, DVM, PHD, DACUP WEIGHER: DIBLELAS HERMON
ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	CIRGAN METGHT RELATIVE TO BODY WETGHT (%)	DREAN TO ARAIN WEIGHT RATIO	ORGAN
ADRENAL (AD)	690.	% 9230 % 9230	.0368	METGHT TAKEN
BRAIN W/STEM (BR)	1.87	% 05C	1.000	,
	26.	% U66:	919.	
SPLEEN (SP)	05°.	. 201 % . 264 %	. 268 1.019	ME 15H1 TAKEN
LIUER (LI)	8.58	3.450 %	4.598	
CLINICAL OBSERVATIONS	ď.	THOLOGY OBSERUATIONS	SZO	HISTOPATHOLOGY
-APPEARED NORMAL	GENERAL INFO	GENFRAL INFORMATION (XX); >NOTE:>EXTERNAL OBSERVATIONS:NONE	PERIBRONCH INFILTRATI	HS (LID): -PERIBRONCHIAL/PERIVASCILAR, INFILTRATION, LYMPHOLD, SLIGHT

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/TITK SYSTEM DITIPHT *** APPENDIX B

INDIVIDINAL ANIMAL SIMMARY REPORT

PRINTFD: 19-may-88 PAGE: 305

STUDY NUMBER: 2399108

RECORDER SID JOHES, DUM, PHD, DADUP 248.6 GRAMS SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE WEIGHER: DRINGLAS HERNDON TERMINAL BODY WEIGHT: PATHOLOGIST: SID JOHES, DUM, PHD, DACUP STUDY WEEK OF DEATH: 14 PROSECTOR: DOUGLAS HERMOTIN DOSE GROUP: 1 STUDY DAY OF DEATH: 96 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL SEX: FEMALE DATE AND TIME OF NECROPSY: 07/15/86 15:11 DATE OF DEATH: 07/15/86 ANIMAL NUMBER: B08396

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRIA, THORACIC (AD), BONE, FEMIN (FE), MONE, STERNIM (SB), BRAIN WASTEM (BR), CECUM (CE), COLON (CD), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORO, THORACIC (TC), DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEIM (IL), ASTRINIM (3F), KIDNEY (KD), LATRIAN (B), LAND (MS), MAND SALIVARY GL (SS), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERUE, SCIATIC (SN), OVARY (DU), PANTREAS (PA), PARATHYROD (FT), PITULTARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NINGLE (SID), THYMUS (TH), THYRODO (TY), TRACHER (TR), LIRINARY BLADDER (LB), UTERUS (LI), ACHIECTED/TAKEN (XM)

ADRENAL, CORTEX (AC), ADRENAL, MEDILLA (AM), ANRIA, THORACTC (AC), BONE, FEMIRE (EE), BONE, STERHIM (SB),
BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORO, CERUICAL (CS), CORO, LUMBAR (LC), CORO, THORACTC (TC),
DUODENUM (OU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEIM (T), JEDINIM (JF), KIDNEY (KD), LACRIMAL GI, EXCL (FD),
LIVER (LI), LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNIM (SF), MISCLE, SKELETAL (SM),
NERUE, SCIATIC (SN), OWARY (NU), PANCREAS (PA), PARATHYROLD (PT), PITHITARY (PT), RECTIM (RF), SKIN (SC),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), THYMUS (TH), THYROLD (TY), TRACHEA (TR), URINARY BLADGER (LB), FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: JTERUS (UT) 꾶

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAUFD ***

APPENDIX H *** PATH/TOX SYSTEM OUTPUT *** SHRCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88 PAGE: 307

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 27991118

ORGAN NAME	ANIMAL NUMBER: B08397 SEX: FEMALE DATE OF DEATH: 07/16/86 STUDY DAY OF DATE AND TIME OF NECROPSY: 07/16/86 9:14 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL	г ОЕАТН	GROVE D JONES	SCHE	DULED, TERMINAL SACRIFICE DAM FILLY WELSHIT 771.1 GRAMS RECORDER: SID JONES, DUM, PHO, DACUP WELGHER: TIM GROUE	ور
(AD) .062 .0229 % .0 .013	ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	DRGAN WEIGHT RF1 ATTUE TO BODY WEIGHT (%)	NEGAN 10 BRAIN WEIGHT RATIO	OREAN STATUS	
1.85	ADRENAL (AD).	. 062	. 0229 % . 0413 %	. 0335		
(47) (47) (48) (49) (40) (40) (40) (41) (41) (42) (42) (43) (43) (43) (43) (44) (45) (45) (45) (45) (46) (46) (47) (48) (48) (48) (48) (48) (48) (48) (48		1.85	.682 %	1.000 .422	, .	
### 1.5	•	. 47	,173 % ,602 %	.254		
AL OBSERVATIONS KIDHEY (KD): -H-PELUIS, DILATED; RIGHT, SLIGHTLY GEHFRAL INFORMATION (XX): NOTE:>EXTERNAL OBSERVATIONS:NOWF	_	6.55	2.416 %	3.541		; ;
KIDMEY (KD): -H-PELVIS, DILATED; RIGHT, SLIGHTLY GENFRAL INFORMATION (XX): >NOTE:>EXTERNAL OBSERVATIONS:NOWF LIMPERS PAR	CLINICAL OBSERVATIC	G G.	D B S E R U A T	у х с	HISTOPATHOLOGY	
	-APPEARED NORMAL	KIDNEY (KD) KIDNEY (KD) KIDNEY SENFRAL INFO NOTE:>EXT	: DILATED; RIGHT, SLIGHTLY RMATION (XX): ERNAL DBSERVATIONS:NONF	KIDNEY (KD) -NEPHROPATH MINIMAL -PELUIS, DI LIMS (LII) : -PERIBERNCH IMS IS TRATI PARATHYROID > SECTION EX	: Y, CHRONIC PROGRESSIVE,- LATATION,-SLIGHT TAL/PERIVASCUI AR, ON, 1 YMPHOID,-SLIGHT (PT) : AMINED; TISSUE NOT PRESE	1111

APPENDIX 8 *** PATH/TOX SYSTEM ONITPUT *** SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88 PACE: 308

STUDY MIMBER: 2599108

INDIVIDUAL ANIMAL SUMMARY REPURT

RECORDER: SID JONES, DUM, PHD, DACUP 271,1 GRAMS SACRIFICE STATUS: SCHEDMLED, TERMINAL SACRIFICE TERMINAL BODY WFIGHT: WEIGHFR: TIM GROVE PATHOLOGIST: SID JONES, DUM, PHD, DACUP STUDY WEEK OF DEATH: 14 PROSECTOR: TIM GROVE DOSE GROUP: 1 STIJDY DAY OF DEATH: 97 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL DATE AND TIME OF NECROPSY: 07/16/86 9:14 SEX: FEMALE DATE OF DEATH: 07/16/86 ANIMAL NUMBER: B08397

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ANRIA, THORACIC (AN), BINE, FFMIR (FE), BORD, THORACIC (TC), BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC), LIVER (LI), DUDDENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HI), ILFIM (II), DENIHIM (JE), LACRIMAL (HI, FXO (FO), LIVER (LN), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROLL, STERNUM (SF), MUSCLE, SKELETAL (SM), NERUE, SCIATIC (SN), QUARY (OV), PANCREAS (PA), PARATHYROLD (PI), PITHITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, GL (ST), THYMUS (TH), THYROLD (TY), TRACHEA (TR), URINARY BLADDER (HB), UTERUS (HI), ^COLLECTED/TAKEN (XW) THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

DRENAL, CORTEX (AC), ADRENAL, MEDILLA (AM), ANRIA, THORACIC (AN), BINE, FFMIR (FE), BURE, STERMIM (SB),
BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), HEUM (H), JEJUKUM (DE), LAGRIMAL G, FKO (FO), LIVER (L)),
LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIDARY GL (SG), MARROM, STERNIM (SF), MISCLE, SKELETAL (SM),
NERUE, SCIATIC (SN), DUARY (DU), PANCREAS (PA), PITUITARY (PI), RECTUM (BF), SKIN (SR), SPEEPH (SP),
STOMACH, GL (ST), STOMACH, NONGL (SU), THYMUS (TM), TRACHEA (TR), URINARY BLADDER (HR), HERRIS (HF) THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

APPENDIX 8 *** PATH/TDX SYSIFM DUITPUT *** SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88 PAGE: 309

STHIPY NEMBER: 2399308

INDIVIDUAL ANIMAL SUMMARY REPORT

RECINDER: SID JUNES, DUM, PHD, DATUP INFILTRATION, LYMPHOLD, -SULGHT 225.8 GRAMS TAKEN WEIGHT TRICEN TAKEN TAKEN TAKEN TAKEN TAKEN STRATES 2 E G B Z - PERTERNACHIAL/PERTUASILII AR HISTOPATHOLDGY SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE - INJECTION SITE, - POSSENT MF I GH I WE LIGHT LIFT I GHT MF 16:41 LET IGHT THE TEHE WEIGHER: BARBARA DAY TERMINAL BROY WEIGHT: CECUM (CF): CING CLU) DREAN TO BRAIN LIETCHT RATTIL .0668 . 8332 1.000 .806 .347 2.719 5. 0. ORSERUALIONS PATHOLOGIST: SID JONES, DUM, PHD, DACUP NUTE: YDARK AREA, POSSIBLE INDECTION -DARK AREA; IN WALL, THE, RED, 5 X STUDY WEEK OF DEATH: 14 >NOTE:>EXTERNAL OBSERUATIONS:NONE DRSAN WEIGHT RELATIVE TO RODY METCHT (%) .0288 % .0580 895. .301 .221 . 780 GENERAL INFORMATION (XX): 2.360 NECROPSY PROSECTOR: MARMARA DAY DOSE GROUP: 1 PATHOLOGY (CE) SITE ABSOLUTE ORGAN WEIGHT STIJDY DAY OF DEATH: 97 CECUM (GRAMS) . 065 .131 .68 1.58 1.965.33 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL DATE AND TIME OF NECROPSY: 07/16/86 13:47 SEX: FEMALE CLINICAL DBSERVATIONS BRAIN M/STEM (BR) DATE OF DEATH: 07/16/86 ANIMAL NUMBER: 808398 (AD) (SP) (S 99 (H) 9 DREAN NAME -APPEARED NORMAL ADREMAL SPLEEN K I DNEY DUARY LIVER HEART

APPENDIX 8 *** PATH/IOX SYSTEM OUTPUT *** SUBCHRONIC TOXICITY STUDY IN RAIS

PRINTED: 12-MAY-88 PAGE: 310

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY MINIER: 2399148

RECORDER: SID JOHES, DUM, PHD, DACUP 225.8 GRAMS SALRIFICE STATUS: SCHEMMED, TERMINAL SACRIFICE WEIGHER: BARBARA DAY TERMINAL BODY WEIGHT: PATHOLOGIST: SID JONES, DUM, PHD, DACUP STUDY WEEK OF DEATH: 14 PROSECTOR: HARBARA DAY DOSE GROUP: 1 STUDY DAY OF DEATH: 97 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL SEX: FEMALE DATE AND TIME OF NECROPSY: 07/16/86 13:47 DATE OF DEATH: 07/16/86 ANIMAL NUMBER: B08398

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRIA, THURACIC (AB), BONE, FFMIR (FE), BONE, STERNIM (SR),
BRAIN WASTEM (BR), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THURACIC (TC), DUDDENIM (DB),
ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), 1 AFRIMAL SI, FKO (FD), LIVER (LD),
LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERRUM (SE),
MUSCLE, SKELETAL (SM), NERUE, SCIATIC (SN), QUARY (DV), PANCREAS (PA), PARATHYRDID (PI), PITHITARY (PI), RECTUM (RE),
SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (SI), STOMACH, NONGL (SU), THYMUS (TH), THYROID (TY),
TRACHEA (TR), URINARY BLADDER (UB), UFFRUS (III), ACOLLECTED/TAKEN (KW) THE FOLLOWING DRIGHNS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ACRIA, THURACIC (AC), BOWE, FEMUR (FE), BOWE, STERNIM CSB),
BRAIN W/STEM (BR), COLON (CO), CORO, CERVICAL (CS), CORO, LUMBAR (LC), CORO, THURACIC (TC), DUDDENUM (CB),
ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJINUM (LE), KIDNEY (KD), LAGRIMAL GI, FYO (FD), LIVER (LT),
LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROM, STERNUM (SE), MISCLE, SKELFTAL (SM),
NERUE, SCIATIC (SN), DVARY (UV), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), RECTUM (RE), SKIN (SK),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADGER (LR), FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: 뽀

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STIDY PROTOCAL) LIFRE SAUFD ***

APPENDIX B *** PATH/TOX SYSTEM OUTPUT *** SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-86 PAINE 311

INDIVIDUAL ANIMAL SHMMARY REPORT

STREE WINNERS 2399109

ANIMAL NUMBER: B08399 SEX: FEMALE DOSE GRUIP: 1 DATE OF DEATH: 07/16/86 STUDY DAY OF DEATH: 97 STUDY DATE AND TIME OF NECROPSY: 07/16/86 14:02 PROSECTOR: BARBA POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SIC	(: FEMALE DOSE GR JOY DAY OF DEATH: 97 '86 14:02 PROSECTOR ' PROTOCOL PATHOLOGI	WEEK C	SCHE TERM	SCHEDBLED, TERMINAL SACRIFICE TERMINAL BNDY WEIGHT: 290.1 GRAMS RECORDER: SID JUNES, DUM, PHD, DACUP WEIGHER: BARBARA DAY	, HELLOP
DRGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN METGHT RATIO	S I L G T S	~ ` r
ADRENAL (AD)	. 183	# 988	5040.	WEIGHT TAKEN	
DUARY (DU)	.125	,0431 %	.06117	METGHT TAKEN	
BRAIN W/STEM (BR)	2.86	.710 %	1.900	LIFTSHT TRKEN	
	.87	. 300 %	.422	WEIGHT TAKEN	
SPLEEN (SP)	86.	% UBC.	.282	LIFTICHT TEKEN	
KIDNEY (KD)	1.82	.627 %	.893	WEIGHT TAKEN	
LIVER (LI)	7.13	2.458 %	3.461	LIFTIGHT TAKEN	F · · ·
CLINICAL OBSERVATIONS	THUT HUT	HOLOGY OBSERUAT INECROPSY	S Z O _	HISTOPATHILOGY	
-APPEARED NORMAL	GENERAL INFO	GENERAL INFORMATION (XX): >NOTE:>EXTERNAL DBSERUATIONS:NOTE:	LUNG (LED): -PFRIBRONCHJAL/PFRIDIINFILTRATION, LYMPH-PNEIMENJIS,-SLIGHT	NG (LU): -PERIBRONCHIAL/PERIUASCULAR, INFILITRATION, LYMPHOLD,-SLIGHT	! ! !

APPENDIX 8 *** PATH/TOX SYSTEM CHITPLIT *** SUBCHRONIC TOXICITY STUDY IN RATS

PRINTFD: 12-MAY-88 PAGE: 312

STHEY HIMBER: 2399108

INDIVIDIDAL ANIMAL SUMMARY REPORT

SACRIFICE STATUS: SCHFOLLFO, TERMINAL SACRIFICE DOSE GROUP: 1

TERMINAL BODY METGHT: 290.1 GRAMS RECORDERS SID JONES, DUM, PHD, DACUP WEIGHER: BARBARA DAY PATHOLOGIST: SID JONES, DUM, PHD, DACUP STUDY WEEK OF DEATH: 14 PROSECTOR: BARBARA DAY DATE OF DEATH: 07/16/86 STUDY DAY OF DEATH: 97 DATE AND TIME OF NECROPSY: 07/16/86 14:02 FROSE POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL SEX: FEMALE

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AD), BURE, FFMIR (FE), BOLF, STERNIM (SB),
BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORD, CERUICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
BUODDENUM (DU), ESDPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JFMINUM (JE), KIDNEY (KD), I ACRIMAL GI, EXD (FD),
LIVER (L1), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MS), MAND SALIVARY GI (SS),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), OVARY (OU), PARICREAS (PA), PARATHYRIID (TT),
PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NINKEL (SL),
THYMUS (TH), THYROID (TY), TRACHEA (TR), LIRINARY BLADDER (11R), LITERIS (111), ATOLIECTED (SM) THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AN), ADRIA, THORACIC (AD), BINE, FEMIR (FF), BONE, SIERNIM (SB),
BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORD, CERUICAL (CS), CORD, LIMBAR (LC), CORD, THORACIC (TC),
DUDDENUM (DU), ESOPHAGUS (ES), EYE (EY), HEARI (HI), ILFUM (IF), ABAINIM (AF), KIDNEY (KD), FERRIMA (AF), FERRIM (AF), MISTLE, SKELFFAL (SM),
LIVER (LI), LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROMA, STERNUM (SF), MISTLE, SKELFFAL (SM),
NERUE, SCIATIC (SN), DUARY (DV), PANCREAS (PA), PARATHYROTO (PI), PITHITARY (PI), RECTUM (RF), SKIM (SK),
SPLEEN (SP), STOMACH, GL (SI), STOMACH, NONGL (SU), THYMUS (TH), THYROTO (TY), TRACHEA (TR), URINARY BLADDER (UR), FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: UTERUS (UT)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STIMY PROTOCOL) WERE SAUFD ***

A** PATH/TOX SYSTEM OUTPUT *** SHRCHRONIC TOXICITY STILDY IN RAIS

PRINTED: 12-MAY-88 PAGE: 313

STUDY NIMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/TITK SYSTEM DIJIPUT ***

PRINTFD: 12-MAY-88 PAGE: 314

> SLIMMARY REPORT INDIVIDINAL ANIMAL

STUDY NUMBER: 9399108

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		1000		· · · · · · · · · · · · · · · · · · ·	POLICIOS (CINTEST OF MONTA OF TOTAL SOCIETY	10.100	
ANIMAL NUMBER: BUSAUD	SEX: PERRILE	ו יאנוואין אנוונו			CALIFORNIA TO THE CONTRACT OF		
DATE OF DEATH: 07/16/86	STUDY DAY OF DEATH: 97		STJOY WEEK O	STIJDY WEEK OF DEATH: 14	TERMINAL BODY WEIGHT: 248.3 GRAMS	248.3 GRAMS	
DATE AND TIME OF NECROPSY: 07/16/86 14:39	07/16/86 14:39	PROSECTOR:	PROSECTOR: BARBARA DAY		RECORDER: SID JONES, DUM, PHD, DACUF	DUM, PHD, DA	5
POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL	TRED BY PROTOCOL	PATH01.0615	r: SID JONES	PATHOLOGIST: SID JONES, DUM, PHD, DACUP	WEIGHER: BARRARA DAY		
			11 11 11 11 11 11 11 11 11 11 11 11 11	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1			1

THE FOLLOWING DRGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AURTA, THORACIC (AC), RONE, FEMUR (FE), BONE, STERNUM (SB),
BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
BUCDENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (11), AFGURUM (AE), KIDNEY (KD), FACRIMAL SI, FXC (FO),
LIVER (L1), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GL (SS),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERUE, SCIATIC (SN), NOARY (NO), PANCREAS (PA), PARATHYRNID (FT),
PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NUNGL (SID),
THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (LB), ACRILECTED (XM)

FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: Ŧ

ADRENAL, CORTEX (AC), ADRENAL, MEDILLA (AM), ADRIA, THORACIC (AD), BIRE, FFMIR (FE), SORT, STERNEM (SE),
BRAIN MASTEM (BR), CECUM (CE), COLON (CD), CORO, CERVICAL (CS), CORD, LIMBAR (LD), CORO, THORACIC (TC),
DUDDENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (LL), KIDNEY (KD), LACREMAN (B., EXO (FU),
LIVER (LI), LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROLL, STERNIM (SE), MISCLE, SKELFTAL (SM),
NERUE, SCIATIC (SN), DUARY (DU), PANCREAS (PA), PITULTARY (PI), RECTIM (RE), SCH (SR), SCHFFN (SP),
STOMACH, GL (ST), STOMACH, NONGL (SU), THYMUS (TH), TRACHEA (TR), URLNARY BLADDER (LB)

ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

APPENDIX B *** PATH/TOX SYSTFM (MITPHT *** SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88 PARE: 315

STUDY NUMBER: 9399109

INDIVIDUAL ANIMAL SUMMARY REPORT

ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO	ORGAN
	******	 	8629	LETERT TREET
HUNENHI, CHO.	116	. 0436 %	0584	WEIGHT TAKEN
BRAIN LIZITEM (BR)	1.96	247 %	1,000	LIFTSHT TAKEN
	. 91	. 345 %	.462	WEIGHT TAKEN
SPLEEN (SP)	.50	.189 №	. 253	METCHT TOKEN
KIDNEY (KD)	2.10	.802 ×	1.074	MEIGHT TAKEN
LIVER (LI)	8.32	3,173 %	4.749	WEIGHT TAKEN
CLINICAL OBSERVATIONS	PATHOL	HOLOGY OBSERUATI NECROPSY	S N O 1	HISTOPATHOLOGY
-APPEARED NORMAL	GENERAL INFO	GENERAL INFORMATION (XX): >MOTE:>EXTERNAL OBSERVATIONS:NONE	KIDNEY (KD): -NEPHREBAINY, CHRMINIMAL. LING (LE): -PERIBRONCHIAL/PFINFILTRATION, LY PARATHYROLD (PT): >SECTION EXAMINED	DNEY (KD): -NEPHRIPATHY, CHRONIC PROGRESSIUF,- MINIMALPERIBRONCHIAL/PERIUASCIM AR, INFILTRATION, LYMPHOID,-SLIGHT NATHYROLD (PT): >SECTION EXAMINED; TISSHE NOT PRESENT

-DILATATION, SLIGHT

APPENDIX 8 *** PATH/IDX SYSTEM (NITPUT *** SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88 PAGE: 316

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY HUMBER: 2399108

TERMINAL BOOY WEIGHT: 262.3 GRAMS RECORDER: SID JOHES, DUM, PHD, DACUP SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE WEIGHER: DOUGLAS HERNOON PATHOLOGIST: SID JONES, DUM, PHO, DACUP STUDY WEEK OF DEATH: 14 PROSECTOR: DONIGLAS HERNDON DOSE GROUP: 1 STUDY DAY OF DEATH: 97 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL DATE AND TIME OF NECROPSY: 07/16/86 15:03 SEX: FEMALE DATE OF DEATH: 07/16/86 NUMBER: 808401

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AGRIA, THORACIC (AG), BGRE, FEMIR (FE), BGRE, STERRUM (SB),
BRAIN MASTEM (BR), CECUM (CD), COLON (CD), CORD, CERUICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
BUDDENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILFIUM (E), JEJINIM (JE), KIDHEY (KD), LATRIMAL RI, EXA (EO),
LIUER (LI), LN, MESENTERIC (MS), LN, GTHER (LN), LUNG (LU), MAMMARY GLAND (MS), MAND SALIUARY GI (SS),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERUE, SCIATIC (SN), GUARY (NU), PANCREAS (PA), PARATHYROID (PT),
PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, GTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NDWAL (SU),
THYMUS (TH), THYROID (TY), TRACHEA (TR), IRINARY ALADOFR (11R), HIERUS (HI), ACCURLACE (SA) THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AURTA, THORACIC (AD), BOWE, FEMIR (FF), BOWE, STERWIM (SB),
BRAIN WASTEM (BR), CECUM (CE), COLON (CD), CORD, CORD, LUMBAR (LC), CORD, THORACIC (TC),
BUODENUM (DU), ESOPHAGUS (ES), FYE (EY), HEART (HT), ILEUM (LT), LETURUM (DE), LACRIMAL RI, FYO (FD), LIVIR (LT),
LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROM, STERNUM (SF), MISCLF, SKELETAL (SM),
NERUE, SCIATIC (SN), DUARY (DU), PANCREAS (PA), PITUITARY (PI), RECTUM (RF), SKIN (SK), SPIFFN (SP),
STOMACH, GL (ST), STOMACH, NONGL (SU), THYMUS (TH), TRACHEA (TR), URINARY BLADDER (UB) FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: 표

*** ALL ORSANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/TIIX SYSTEM MITPUIT *** APPENDIX 8

PRINTED: 12-MAY-88

INDIVIDUAL ANIMAL SUMMARY REPORT

STHDY HIMRER: 2399108

SACRIFICE STATUS: SCHFOLLED, FFRMINAL SACRIFICE PATHOLOGIST: SID JONES, DUM, PHD, DACUP 1: 95 STUDY WEEK OF DEATH: 14 PROSECTOR: DOWGLAS HERMORN DOSE GROUP: 2 SEX: FEMALE DUS STUDY DAY OF DEATH: 95 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL DATE AND TIME OF NECROPSY: 07/14/86 10:00 DATE OF DEATH: 07/14/86 ANIMAL NUMBER: B08422

TERMINAL BROY METGHT: 260.3 GRAMS RECORDER: STO JONES, DUM, PHD, DACUP WEIGHER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

-APPEARED NORMAL

-NEPHRIIPAIHY, CHRONIC PROGRESSIVE,--FOCI OF MONONICLEAR CELLS, -MINIMAL THE ILLIRATION, LYMPHOLID, SILVENI -PERTBRONCHTAL ZPERTUASCHLAR HISTOPATHOLOGY KIDNEY (KD) : 1,10ER (1.1) : 1 11 11 11 11 MINIM **OBSERUATIONS** -ELECTRON MICROSCOPY SAMPLE; LIVER ANDTE: SEXTERNAL DRSERVATIONS: NONE GENERAL INFORMATION (XX) : NECROPSY ~COLLECTED/TAKEN (XW) PATHULOGY CLINICAL DBSERUATIONS

THE FOLLDWING ORGANS WERE UNREMARKABLE AT NECROPSY:

THE FOLLDWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AD), BINE, FEMUR (FE), BINE, STERNUM (SB),

BROAIN W./STEM (BR), CECUM (CE), COLON (CO), CARD, CATTO, COLON (CO), LACRIMAL GI, EXO (FD),

BURDIN W./STEM (BR), CECUM (CE), EVE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIONEY (K), LACRIMAL GI, EXO (FD),

LIUER (L), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LI), MAMMARY GI AND (MS), MAND SAI IVARY (R, (SG), MUSCLE, SKELETAL (SM), NERUE, SCIATIC (SN), DUARY (DV), PANCREAS (PA), PARRATHYROID (PI),

PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (SI), STOMACH, FINAL (SI),

THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UI)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

APPENDIX 8 *** PATH/TOX SYSTEM OUTPUT *** SUBCHRONIC TOXICITY STUDY IN RAIS

PRINTED: 12-MAY-88 PAGE: 318

INDIVIDIJAL ANIMAL SIJMMARY REPORT

PAGE: 318

STIJDY NUMBER: 2399108

DOSE GROUP: 2 SACRIFICE STATUS: SCHEDULED, TERMINAL SALRFICE H: 95 STUDY WEEK OF DEATH: 14 TERMINAL BODY WFIGHT: 259.0 GRAMS PROSECTOR: DOUGLAS HERDON PROSECTOR: DOUGLAS HERDON PATHOLOGIST: SID JONES, DOM, PHD, DACUP WEIGHER: NOT REQUIRED BY PROTOCOL
DOSE GROUP: 2 SACRIFICE STATUS: DEATH: 95 STUDY WEEK OF DEATH: 14 PROSECTOR: DOUGLAS HERDON PATHOLOGIST: SID JONES, DVM, PHD, DACUP
ANTMAL NUMBER: 808423 SEX: FEMALE DOSE DATE OF DEATH: 07/14/86 STUDY DAY OF DEATH: 95 DATE AND TIME OF NECROPSY: 07/14/86 11:15 PRINSEC POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL PATHOL.

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRIA, THORACIC (AD), BONE, FEMUR (FE), BONE, STERNIM (SB),
BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CHRO, CERVICAL (CS), CHRO, LUMBAR (LC), CHRO, THURACIS (ES),
DUDDENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNIM (JE), KIDNEY (KO), LACRIMAL GL, EXO (ED),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LING (LU), MAMMARY GLAND, MAND SALIUARY GL. (SG),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERUE, SCIATIC (SN), QUARY (OU), PANCREAS (PA), PARATHYROID (PT),
PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPI EN (SP), STOMMACH, GL (ST), STOMMACH, MINUS (SI),
THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT) THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: KIDNEY (KD)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STHDY PROTOCH) WERE SAUFD ***

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/TOX SYSTEM DUTPUT *** APPENDIX B

PRINTED: 12-MAY-BH

STUDY NUMBER: 2399108

INDIVIDIBL ANIMAL SUMMARY REPURT

TERMINAL BODY METGHT: 272.9 GRAMS RECORDER: SID JOHES, DUM, PHO, DADUP WEIGHER: NOT REQUIRED BY PRITOCHI SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE PATHOLOGIST: SID JONES, DUM, PHD, DACUP STUDY WEEK OF DEATH: 14 PROSECTOR: DOLIGLAS HERNOON DOSE GROUP: 2 STUDY DAY OF DEATH: 95 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL DATE AND TIME OF NECROPSY: 07/14/86 14:00 SEX: FEMALE ANIMAL NUMBER: 808424 DATE OF DEATH: 07/14/86

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

-FORT OF MINIMUM EAR CFU S, - MINIMA INFILTRATION, LYMPHOID, -SLIGHT -PERTHERMENTAL /PERTUASCHLAR, HISTOPATHOLOGY LIUER (LI): CONSTRUCTION : PATHOLOGY DRSERVATIONS ^COLLECTED/TAKEN (XW) :
-ELECTRON MICROSCHPY SAMPLE; LIUFR >NOTE:>EXTERNAL ORSERVATIONS:NONE GENERAL INFORMATION (XX) : NECROPSY CLINICAL DBSERVATIONS -APPEARED NORMAL

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

AORENAL, CORTEX (AC), ADRENAL, MEDILLA (AM), AFRIA, THORACIC (AC), CORO, LUMBAR (LC), CORO, THORACIC (TC),

BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORO, LUMBAR (LC), CORO, THORACIC (TC),

BRAIN WASTEM (BR), CECUM (CE), EYE (EY), HEART (HT), ILFIM (IL), DELIBNIM (DE), RIDREY (RD), LASSITANCE (ES), MISCLE, SKELETAL (SM), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GE (ST),

MARROW, STERNUM (SE), MISCLE, SKELETAL (SM), NFRUE, SCIATIC (SM), OUARY (DU), PANICHE AS (FA), STOMACH, GE (ST), STOMACH, NORMEL (SM),

THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (18), LIFERIS (LT)

FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: KIDNEY (KD) 프

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PRITHER) LERE SAUED ***

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/INX SYSTEM DIITPIIT *** APPENDIX B

PRINTED: 12-MAY-88

STIERY 18 MRFR: 2399108

INDIVIDINE ANIMAL SUMMARY REPORT

RECORDER: SID JOHES, OWM, PHD, DACOP TERMINAL BRIDY METCHT: 261.3 GRAMS SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE WETGHER: TIM GROUE PATHOLOGIST: SID JONES, DUM, PHD, DACUP STUDY WEEK OF DEATH: 14 PROSECTOR: TIM GROUE DOSE GROUP: 2 DATE OF DEATH: 07/14/86 STUDY DAY OF DEATH: 95
DATE AND TIME OF NECROPSY: 07/14/86 9:45 PROSE POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL SEX! FEMALE ANIMAL NUMBER: 808425

ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	DRGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN LEIGHT RATIO	ORGAN Status
ADRENAL (AD)	0.00.	% US3U.	. 8326	METCHT TAKEN
DUARY (0U)	.116	. 0444 X	.0630	WEIGHT TAKEN
BRAIN W/STEM (BR)	1.84	2 4 11√.	1.000	METGHT TAKEN
HEART (HT)	06.	. 344 %	.489	MEIGHT TAKEN
SPLEEN (SP)	.51	. 195 %	555.	LIFIGHT TAKEN
KIDNEY (KD)	1.80	% 689°	.978	WEIGHT TAKEN
LIVER (LI)	10.14	3.8A1 %	5.511	METCHT TAKEN
CLINICAL OBSERVATIONS	T H U C	ATHOLOGY OBSERVATIONS NECROPSY	S 7 0	HISTOPATHOLOGY
-APPEARED NORMAL	GENERAL INFORMA NOTE: YEXTERN	GENERAL INFORMATION (XX);	LUNG (LID) : -PERTHERNCH INFILTRETTI	NG (LID :

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

AORENAL, CORTEX (AC), ADRENAL, MEDIALA (AM), ADRIA, THIRACIE (AC), BORD, LIMBAR (LC), CORD, THORACIE (TE),

BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORD, CERUICAL (CS), CORD, LIMBAR (LC), RIDIALY (RD), FARIMAL RE, FAM (FID),

DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (LI), MANMARY GLAND (MS), MAND SALIVARY GLAND (RD), CANALLYCHIN (FID).

LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MS), MAND SALIDARY GL (SR), MARROW, STERNUM (SE), MUSCLE, SKELFTAL (SM), HERUE, SCIATIC (SN), DVARY (MU), PANCREAS (PA), PARATHYRID (FT), PITULIARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMMCH, GL (ST), STOMMCH, NINGL (SH), THYMUS (TH), THYROID (TY), TRACHEA (TR), HRINARY RLADDER (MR), HTFRUS (HI), ACRIFED TARKEN (XL)

FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: Ŧ

KIDNEY (KD), LIVER (LI)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STRINY PROTRIGAL) WERE SAUFD ***

SUBCHRONIC TOXICITY STUDY IN RATS *** PATHZINX SYSTEM NUTPUT *** APPENDIX 8

PRINTED: 12-MAY-80 PAGE: 391

STIDY HUMBER: 2399188

INDIVIDUAL ANIMAL SIMMARY REPORT

SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE PATHOLOGIST: SID JONES, DUM, PHD, DACUP STUDY WEEK OF DEATH: 14 PROSECTOR: BARBARA DAY DOSE GROUP: 2 STUDY DAY OF DEATH: 95 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL DATE AND TIME OF NECROPSY: 07/14/86 14:33 SEX: FEMALE DATE OF DEATH: 07/14/86 ANIMAL NUMBER: B08426

RECTIRDER: SID JANES, DUM, PHD, DACUP WELISHER: NOT REQUIRED BY PROTOCOL TERMINAL BODY WEIGHT: 234.1 GRAMS

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

CLINICAL OBSERVATIONS

-APPEARED NORMAL

PATHOLOGY OBSERVATIONS NECROPSY

^COLLECTED/IAKEN (XW):
-FLECTRIN MICROSCOPY SAMPLE; LIUFR GENERAL INFORMATION (XX) :

INFILTRATION, LYMPHOID, -SLIGHI

-PERTHRENEMIAL/PERTUASION AR

LUNG (LU) :

HISTOPATHOLOGY

MOTE: SEXTERNAL DBSERUATIONS: NONE

THE FOLLOWING ORGANS MERE UNREMARKABLE AT NECROPSY:
ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AD), BONE, FEMUR (FE), BONE, STFRWIM (SB),
ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (CS), CHRD, FLWINGER (CC), CHRD, THERACIC (TC),
BODDINUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEDUNUM (AC), MAND SALIVARY (B), LACRIMAL (B),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LING (LU), MANDARY (AC), MAND SALIVARY (B), PARCHIYROLO (PT),
PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPLFEN (SP), STRMACH, MS (SI), STRMACH, MS (SI), THYMUS (TH), THYMUS (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT)

FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: KIDNEY (KD), LIVER (LI) 포

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STIMY PROTOCOL) LIERE SAUFD ***

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/TOX SYSTEM DUTPUT *** APPENDIX B

PRINTED: 12-MAY-88 PAGE: 322

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NIMBER: 2399108

ANIMAL NUMBER: B08427 SEX: FEMALE DATE OF DEATH: 07/14/86 STUDY DAY OF DATE AND TIME OF NECROPSY: 07/14/86 12:56 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL	DEATH	DOSE GROUP: 2 SACRIFICE STATUS: 4: 95 STINY MEEK OF DEATH: 14 PROSECTOR: DOMSLAS HERNDON PATHOLOGIST: SID JONES, DUM, PHD, DACUP	SCHE 1FRM	SCHEDULED, TERMINAL SACRIFICE TERMINAL BIEN WEISHI: 275.2 GRAMS RECORDER: SID JONES, DUM, PHD, DAIJUP WEIGHER: DOMELAS HERNOM
ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	CIRGAN IN ERAIN WEIGHT RATIO	ORGAN STATUS
ADRENAL (AD)	.053	0194 %	0289	METGHT TAKEN
BRAIN WASTEM (BR)	1.85	.673 %	1.000	WFIGHT TAKEN
	.88	. 321 %	87.4	LIFTGAT TEKEN
SPLEEN (SP)	89.	.24B %	.369	WEIGHT TAKEN
KIDHEY (KD)	1.81	% 659.	666.	METCHT TAKEN
LIVER (LI)	7.70	2.798 %	4.157	WFIGHT TAKEN
CLINICAL OBSERUATIONS		ATHOLOGY OBSERUATIONS NECROPSY		HISTIPATION ORY
-APPEARED NORMAL	GENERAL INFI	GENERAL INFORMATION CXX): >NOTE:>EXTERNAL OBSERVATIONS:NONE	PERTBROWSH PERTBROWSH THE FL TRATE	NG (11) : -PERIBRONCHIAL/PERIUASCULAR, THE H TRATION, LYMPHOLD,-MINIMAL

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AGRIA, THORACIC (AD), BTHE, FEMIR (FE), BTHE, STERHUM (SB), BRAIN WASTEM (BR), CECUM (CE), COLON (CD), CORO, CERVICAL (CS), CORO, LUMBAR (LC), CORO, THORACIC (TC), DUDDENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), ASTRUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), MAMMARY GLAND (MS), MAND SALIDARY GL (SR), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NFRUE, SCIATIC (SN), OVARY (NU), PARCKES (FA), FARATHYROID (FI), PILUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, MUBBL (SID, THYMUS (TH), THYROID (TY), TRACHEA (TR), URIMARY BLADDER (1H), HIFRUS (TI), ACHIECTED/TAKEN (XB) THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: KIDNEY (KD), LIVER (L1)

^{***} ALL ORGANS/TISSUES (REQUIRED TO RE HARVESTED PER THE STUDY PROTOCOLD MEDE SAUFD ***

SUBCHROWIC TOXICITY STUDY IN RATS *** PATH/TOX SYSTEM DITIPUT *** APPENDIX 8

PRINTED: 12-MAY-88

STIDY NIMBER: 23991118

INDIVIDUAL ANIMAL SUMMARY REPURT

808428 07/15/86 IF NECROPSY: 07/ R: NOT REGUIRED	DEATH:	DOSE GROUP: 2 SACRIFICE STATUS: 1:96 STHOY WEEK OF DEATH: 14 PROSECTOR: TIM GROUE PATHOLOGIST: SID JONES, DWM, PHD, DATUP	SCHE	SCHEDILED, TERMINAL SACRIFICE IFRMITAL FODY WEIGHT: 275.9 GRAMS RECORDER: SIO JONES, DUM, PHO, DACUP WEIGHER: I'M GROUE
ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	NRGAN METSHT RELATIVE TO BODY WEIGHT (%)	DRGAN TO BRAIN WEIGHT RATIO	ОКБАИ STATUS
ADRENAL (AD)		.0245 %	.0363	MFIGHT TAKEN
	.123	. 11445 %	. 1663	
BRAIN WYSTEM (BR)	1.86	35 47.9°	1.018	METOTAL TRACES
REAKI (HI)	00 c	177. 201	5 60 60 60 60 60 60 60 60 60 60 60 60 60	
KIDNEY (KD)	1.54	. 45 4 00 4 0 0 4 0 0 7	6.58	-
LIVER (LI)	6.09	2.207 %	3.278	WEIGHT TAKEN
CLINICAL OBSERVATIONS	C C	THOLOGY OBSERUATIONS NECROPSY	SZO	HISTOPATHOLOSY
	GENFRAL INFORM	NERAL INFORMATION (XX):	PERTBRONCY - PERTBRONCY THE UT RATI	NS (11) : -PERIBRONCHIAL/PERIUASCULAR, INFULTRATION, LYMPHOLD,-SLUSHI

THE FOLLOWING DRISANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CTRTEX (AC), ADRENAL, MEDILLA CAN), AIRTA, IHDRACIC (AC), BORE, FEMIR (FE), BORE, STERNIM (SB),
BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LIMBAR (LC), CORD, THORACIC (TC),
BUGDENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), AFMIRIM (AC), KIONEY (KD), LACRIMAL B, FXO (FD),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY G. (SR),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NFRUE, SCIATIC (SN), TOARY (NO), PANTORES (PR), PARAIHYROTO (PI),
PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMMOCH, G. (ST), STOMMOCH, G. (ST), STOMMOCH, G. (ST), THYMUS (TH), THYMUS (TH), THYMUS (TH), HERBER (SI), HERBER (SI), ACOURTED/TAKEN (XM)

FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: KIDNEY (KD), LIVER (LI) 11

^{***} ALL ORGANS/IISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOM) WHAN GAUFD ***

APPENDIX 8 *** PATH/TINX SYSIFM OUTPUT *** SUBCHRONIC TOXICITY STUDY IN RAIS

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STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL SIMMARY REPORT

DATE OF DEATH: 07/15/86 STUDY DAY OF DATE AND TIME OF NECROPSY: 07/15/86 15:04 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL	DEATH: 9	I: 96 STUDY WEEK OF DEATH: 14 PRESECTOR: BARBARA DAY PATHOLOGIST: SID JONES, DUM, PHD, DACUP	TERM	METGHER: BARRARA DAY METGHER: BARRARA DAY
(1RGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BIDY WEIGHT (%)	ORGAN TO BRAIN MEIGHT RATIO	GREAN STATHS
ADREMAL (AD)	. 160	\$ 9550.	. 11351	METCHT TAKEN
BRAIN W/STEM (BR)	2.08	.726 %	1.000	
HEART (HT)	. 88	307 %	. 423	WEIGHT TAKEN
SPLEEN (SP)	. 73	255 W	. 351	METCHT TAKEN
	2.27	792 %	1.091	WEIGHT TAKEN
LIVER (LI)	7.80	2.722 %	3,250	METSHT TAKEN
CLINICAL OBSERVATIONS	G	HOLOGY OBSERUATION NECROPSY	S Z C	HISTOPATHOLOGY
-APPEARED NORMAL	KIDNEY (KD): -PELUIS, DILATED; LEFT, SLIGHTLY UTERUS (UT): -LUMEN, FLUID; BI GENERAL INFORMATION >NOTE:>EXTERNAL GI	KIDNEY (KD): -PELUIS, DILATED; RIGHT, MIDERALELY; LEFT, SLIGHTLY UTERUS (UT): -LUMEN, FLUID; BOTH HORNS, CLEAR GENERAL INFORMATION (XX): >NOTE:>EXTERNAL OBSERVATIONS:NONE	[KIDNEY (KD): -PELUER (LI): -FIDER (LI): -FIDER (LI): -FIDER (LI): -PERIBRONCHIAL/PERIUASONLAR; INFILTRATION, LYMPHOLD,-SI (GHT): -PERIBRONCHIS,-MINIMAL.

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRIA, THORACIC (AC), BONE, FEMURE (FE), BONE, STERNUM (SB),
BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LIMERRY (LD), CARD, LACRIMAL GL, EXO (FD), LIVER (LI),
LN, MESENTERIC (MS), LN, OTHER (LN), LING (LD), MAMMARY GLAND (MS), MAND SALIGARY AL (SS), MARROLL, STERNUM (SF),
MUSCLE, SKELETAL (SM), NERUE, SCIATIC (SN), OUGRY (OU), PANCREAS (PA), PARATHYROLD (PT), PITHITARY (PT), RETIEM (RE),
SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMMOTH, GL (ST), SIDMACH, NORBER (SD), DETRICALD, HERRODE (TN),
TRACHEA (TR), URINARY BLADDER (UB), ADDLLECTED/TAKEN (XW)

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECKUPSY:

^{***} ALL ORGANS/TISSIJES (REQUIRED TO BE HARVESTED PER THE STIMY PROTOCIN.) WERE SAVED ***

APPENDIX 8 *** PATH/TOX SYSTEM DUTEUT *** SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-80 PACE: 195

SHEW MINISTERS 2399189

INDIVIDUAL ANIMAL SHMMARY REPORT

TINAL BODY WEIGHT: 229.7 GRAMS RECORDER: SID JONES, DUM, PHD, DACUP INFILTRATION, LYMPHOTO, - SLIGHT WEIGHT TAKEN TAKEN TAKEN TAKEN TOKET. TAKEN TRKEN STATES - PERTERIMENTAL / PERTUASEMEAR HISTOPATHOLOGY TERMINAL SACRIFICE WEIGHER: DOUGLAS HERNDON ME LOST LE IGHT WE LOHE 1451 FM LE IGHT INF I SHT TERMINAL BRIDY WEIGHTE CUMS (LLU) : DRIAN TO BRAIN WEIGHT RATIO SACRIFICE STATUS: SCHEDMIFD, .0377 . 0544 0.00 .982 1.040 .426 4.319 OBSERUALLINS PATHOLOGIST: SID JONES, DUM, PHD, DAILUP STINDY WEEK OF DEATH: 14 ORGAN METGHT RELATIVE VACIETY EXTERNAL DRISFRUATIONS NOTE TO RODY METCHT (%) PROSECTOR: DOMESTAS HERNDEN .0325 .0469 .367 400 . B47 .862 •• \$ NECROPSY GENERAL INFORMATION DOSE GROUP: 2 PATHOLOGY ABSOLUTE ORGAN WEIGHT STUDY DAY OF DEATH: 96 (GRAMS) . 0.75 .108 1.94 1.98.84 . 51 8.55 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL SEX: FEMALE DATE AND TIME OF NECROPSY: 07/15/86 14:45 CLINICAL DBSERUATIONS DATE OF DEATH: 07/15/86 ANIMAL NUMBER: B08430 BRAIN W/STEM 9 (SP) 9 Œ 900 5 ORGAN NAME -APPEARED NORMAL ADRENAL SPI.EEN KIDNEY CUARY HEART LIUER

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AN), ADRIA, THDRACIC (AD), BONE, FEMUR (FE), BONE, STERNIM (SB),
BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORD, CERUIGAL (CS), CORD, LIMBAR (LC), CORD, THORACIC (TC),
BUGDENUM (DU), ESCHHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIONEY (KO), LAFRIMAL GL, EXD (ED),
LIVER (LI), LN, MESENTERIC (MS), IN, OTHER (LN), LING (LU), MAMMARY GLAND (MS), MAND SALIUARY GLOSS, MANDLE, SKELETAL (SM), NERUE, SCIATIC (SN), QUARY (QU), PANGREAS (PA), PARATHYRHIO (PI),
PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPI FFN (SP), STORACH, GL (ST), STUMBCH, NONER, (SU),
THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT), ACOLLECTED/TAKEN (XW) THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCIPIC FXAMINATION: KIDNEY (KD), LIVER (LI)

^{***} ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WARE SAUCH ***

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/TINX SYSTEM DUTPINT *** APPENDIX B

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INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 239910R

257.3 GRAMS SACRIFICE STATUS: SCHEDULED, VERMINAL SACRIFICE TERMINAL BODY WEIGHT: PATHOLOGIST: SID JONES, DUM, PHD, DACUP STUDY WEEK OF DEATH: 14 PROSECTOR: HARBARA DAY DOSE GROUP: 2 DATE AND TIME OF NECROPSY: 07/15/86 9:24 PRIGS POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL SEX: FEMALE ANIMAL NUMBER: 808431

RECORDER: SID JEWES, DUM, PRD; DAEUP MEIGHER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

OBSERUATIONS NECROPSY PATHOLOGY CLINICAL OBSERVATIONS

-APPEARED NORMAL

FIRM, NODULAR, TAN, RED, 1.8 X 1.6 X -MASS-UFL) LEFT AXILLA, THE, SEMI-MAMMARY GLAND (MIS) :

-ELECTRON MICROSCOPY SAMPLE; LIVER 0.6 CM, CUIT SURFACE: SAME GENERAL INFORMATION (XX) : COLLECTED/TAKEN (XW) :

-M-ADENOCARCINOMA, -NEOPLASM PRESENT

INFILTRATION, LYMPHOID, - SI IGHT -PFRIPROBEHIAL APPRICASCULAR.

CONG COD :

MAMMARY (3 AND) (MS) :

HISTOPATHOLOGY

>NOTE:>FXTERNAL DRSERUATIONS:MASS-UFL IN CAPSULE #1

GENERAL INFORMATION :

>TISSUE MASS:> #1; 1.0640 GRAMS; UFL

ì

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRIA, THORACIC (AD), BONE, FEMUR (FE), BONE, STERNIM (SB),
BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CHRO, CERVICAL (CS), CORD, LIMBAR (LC), CHRO, THORACIC (TC),
DUDDENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIONEY (KO), LACRIMAL GL, EXO (FO),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LLMG (LID), MAND SALIVARY GL (SS), MARRIAL, STERMIM (SE),
MUSCLE, SKELETAL (SM), NERUE, SCIATIC (SN), DUMRY (DU), PANCREAS (PA), PARATHYROID (PT), PITULIARY (PI), RECTUM (RF),
SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (SI), STOMACH, HUBBIL (SU), HYMIS CH), HYRGID (TY), THE FOLLOWING ORGANS WERE UNRETHARKABLE AT MECROPSY: TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT)

FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: KIDNEY (KD), LIVER (LI) *** ALL ORGANS/TISSUES (REQUIRED TO BE MARVESTED PER THE STUDY PRETRICH) WERE SAVED ***

A** PATH/IDX SYSTEM NUTPUT *** SUBCHRONIC TOXICITY STUDY IN RAIS

PRINTED: 12-MAY-88 PAGE: 307

STHDY NUMBER: 2399118

INDIVIDUAL ANIMAL SHYMARY REPORT

ANIMAL NUMBER: B08432 SEX: FEMALE DATE OF DEATH: 07/16/86 STUDY DAY OF DATE AND TIME OF NECROPSY: 07/16/86 9:38 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL	: БЕАТН	C Di	SCHF TERM	SCHEDULED, TERMINAL SACRIFICE TERMINAL BOOY WEIGHT: 254.6 GRAMS RECORDER: SID AINES, DUM, PHD, DACUP WEIGHER: IIM GROVE
DRGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	DRSAN WEIGHT RELATIVE TO RODY WEIGHT (%)	ORSAN TO BRAIN WEIGHT RATIO	ORGAN Status
			1 1 1 1 1	
ADRENAL (AD)	.057	. D224 W	9620.	LETSHIT TAKEN
UND ABOUT	.112	.0440 %	.0619	WEIGHT TAKEN
BRAIN MASTEM (BR)	1.61	2011 20	1.686	LIETGHT TAKEN
	252	₹ 565	.414	WEIGHT TAKEN
(ds) Nation		% 095°	C85.	METCHT TAKEN
KIDNEY (KD)	1.60	.628 %	.894	WEIGHT TAKEN
LIVER (LI)	00.9	2.357 %	3.315	MEIGHT TAKEN
CLINICAL OBSERVATIONS	G G	THOLOGY OBSERVATIONS NECROPSY		HISTOPATHOLOGY
-APPEARED NORMAL	GENERAL IN	GENERAL INFORMATION (XX):	KIDNEY (KD): -NEPHRIPATHY MINIMAL	DNEY (KD): -NEPHRIPATHY, CHROKIC PROGRESSIVE,- MINIMAL

AORENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AGRIA, THURACIC (AG), BURE, FFMIR (FF), BIRE, SIFREM (SB),
BRAIN WASTEM (BR), DECUM (CD), COLON (CD), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THURACIC (TC),
BUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), HEHM (H), REJINAM (LF), KIDNEY (KD), LASTEM (SS),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GL (SS),
MARROW, STERNUM (SE), MUSCLE, SKELFTAL (SM), NERUE, SCIATIC (SN), TOWARY (BU), PARCINEAS (PA), PARCINEAS (PA), PARCINEAS (PA), SKIN (SK), SKIN (SK), SKIN (SK), SKIN (SK), SKIN (SK), LRIMARY READDER (BP), HERRIS (HI), ACHIECH (CM), THYROLD (TY), TRACHEA (TR), URINARY READDER (HB), HERRIS (HI), ACHIECH (CM) THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

-FOCI OF MONONICLEAR CELLS, -MINIMA

: (:1)

INFILTRATION, LYMPHOID, -SLIGHT

-PERTBRONCHIAL /PFRTUASION AR

LING. CLD :

^{***} ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PRINTORI) WHE SAUFD ***

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/TOX SYSTEM DUTPIT *** APPENDIX 8

PRINTED: 12-MAY-88 PAISE: 32B

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY MIMRER: 2399108

TERMINAL BROY WEIGHT: 265.9 GRAMS RECRRDER: STO JUHES, DUM, PHD, DACUP SACRIFICE STATUS: SCHEDULFD, TERMINAL SACRIFICE PATHOLOGIST: SID JONES, DUM, PHO, DACUP STIJDY WEEK OF DEATH: 14 PROSECTOR: TIM GROUE DOSE GROUP: 2 STUDY DAY OF DEATH: 96 POST-FIX WEIGHER! NOT REGUIRED BY PROTOCOL DATE AND TIME OF NECROPSY: 07/15/86 10:52 SEX: FEMALE DATE OF DEATH: 07/15/86 ANIMAL NUMBER: 808433

WEIGHER: NOT REQUIRED BY PRITTING

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

PATHOLOGY CLINICAL OBSERVATIONS

NECROPSY

OBSERUATIONS

INFILTRATION, LYMPHOID, -SLIGHT -PERTHRUMINIAL /PERTUASION AR LUNG (LIJ) :

HISTOPATHOLDGY

GENERAL INFORMATION (XX):

-ELECTRON MICROSCOPY SAMPLE; LIVER

COLLECTED/TAKEN (XL)

-APPEARED NORMAL

NOTE: YEXTERNAL OBSERVATIONS: NOTE:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRTA, THORACIC (AD), BINE, FEMUR (FF), BONE, STERNIM (SB), BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORD, CREVICAL (CS), CIRD, LIMBAR (LC), CORD, THORACIC (TC), DUDDENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), DEJUNIM (JE), KIDNEY (KO), LACRIMAL GL, EXO (ED), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LIMB (LI), MAMMARY GLAND (MG), MAND SALVARY GL (SG), MASCLE, SKELETAL (SM), NENUE, SCIATIC (SN), DUARY (OU), PANCREAS (PA), PARATHYROLD (PI), PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN (SK), SPIFEN (SP), STEMACH, GL (ST), STEMACH, GL (ST), STEMACH, MANAL (SU), THYMUS (TH), THYMUS THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: KIDNEY (KD), LIUER (LI) 뿔

*** ALL ORGANSZTISSUES (REQUIRED TO BE HARUESTED PER THE STILDY PROTOCOL) LAFRE SAUTD ***

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/10X SYSTEM DUTPIT *** APPENDIX 8

PRINTED: 19-MAY-88

STUDY MUMPER: 9399108

INDIVIDIAL ANIMAL SHMMARY REPORT

SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE PATHOLOGIST: SID JONES, DUM, PHD, DACUP H: 96 STUDY WEEK OF DEATH: 14 PROSECTOR: TIM GROVE DOSE GROUP: 2 DEATH: 96 STUDY DAY OF POST-FIX WEIGHER: NOT REGUIRED BY PROTOCOL AND TIME OF NECROPSY: 07/15/86 11:38 DATE OF DEATH: 07/15/86 ANIMAL NUMBER: B08434

TERMINAL BODY WEIGHT: 241.1 GRAMS RECORDER: SID JONES, DUM, PHD, DACUP WEIGHER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

CLINICAL OBSERVATIONS

-APPEARED NORMAL

OBSERVATIONS NECROPSY PATHOLOGY

-ELECTRON MICROSCOPY SAMPLE) LIUFR GENERAL INFORMATION (XX): ~COLLECTED/TAKEN (XW) :

ANDTE:VEXTERNAL DBSERVATIONS:NOWE

INFILTRATION, LYMPHOID, -SLIGHT

-PERTERBER HITH FALZPERTUASSULLAR

(C)) :

HISTOPATHOLOGY

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRIA, THORACIC (AD), BONE, FEMURY (FE), BONE, STERNIM (SB),
BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CRND, CRND, CHIMBAR (FC), CRND, THORACIC (TC),
BUDDENUM (DU), "ESOPHAGUS (ES), EYE (EY), HEART (HI), ILEUM (IL), JEJUNUM (JE), KIONEY (KD), LACRIMAL GL, EXO (EO),
LIVER (LI), LN, MESENTERIC (MS), IN, OTHER (IN), LUNG (LU), MAMMARY GLAND (MS), MAND SALJUARY GL (SS),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERUE, SCIATIC (SN), DUARY (DU), PANCREAS (PA), PARATHYROLD (PI),
PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPIER (SP), STIMMACH, GL (ST), STIMMACH, HOWAGH (SH),
THYMUS (TH), THYROLD (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT) THE FOLLOWING ORGANS WERE UNREMARKABLE AT MECROPSY:

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: KIDNEY (KD), LIVER (LI) *** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STIIDY PROTOKAR) 14:18 SAUCD ***

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/TOX SYSTEM DITIFILE *** APPENDIX 8

PRINTFD: 12-MAY-RE PAISE: 330

STUDY NUMBER: 9399188

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: 808435 SEX: FEMALE DATE OF DEATH: 07/16/86 STUDY DAY OF OFTE AND TIME OF NECROPSY: 07/16/86 13:48 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL	· DEATH	GROUP: 2 STUDY WEFK O TOR: TIM GROUE OGIST: SID JONES	-	SCHFORLED, TERRITIAL SACRIFICE TERMINAL BODY WEIGHT: 241.5 GRAMS RECORDER: SID JONES, DUM, PHD, DACUP WEIGHER: IIM GROUE
CIRGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	T ORGAN WEIGHT RELATIVE TO RODY WEIGHT (%)	ORGAN TO BRAIN JEISHT RATIB	DRGAN STATUS
	1 1 1 6 5 2 4 3	1 1 1 1 1 1 1 1	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
ADREMAL (AD)	8 20	% 全6至0"	.በ38ሉ	WEIGHT TAKEN
DUARY (DU)	.106	.0439 %	.0525	WEIGHT TAKEN
BRAIN W/STEM (BR)	2.02	% 928°	1,080	LIGHTSHIT TAKEN
	۴.	327 %	.391	WEIGHT TAKEN
SPLEEN (SP)	. 42	174 %	24R	LIFT TAKEN
KIDNEY (KD)	1.96	.812 %	.970	WEIGHT TAKEN
LIVER (LI)	7.76	3.213 %	3.842	UFICHT TAKEN
1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1)	1
CLINICAL OBSERVATIONS		NECROPSY		HISTOPATHOLOGY
-APPEARED NORMAL	KIDNEY (KD): -PELUIS, DILG GENERAL INFORM	KIDNEY (KD): -PELUIS, DILATED; RIGHT; MIDFRATELY GENERAL INFORMATION (XX): >NDTE:>FXTERNAL DASERUATIONS:NOWE	; X	ONEY (KO): -NEPHKHPATHY, CHRONIC PROGRESSIVE;- MINIMALPELUIS; DIFATATHY,-MCDFRATE

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AGRIA, THORACIC (AD), EDNE, CEMIR (SE), BORE, STERBER (SB),

BORENIA MASTEM (BR), CECUM (CC), CORO, CERUTCAL (CS), CORD, LIMBAR (LC), CORD, THURACIC (TC),

BURDAIN MASTEM (BR), CECUM (CC), CORO, CERUTCAL (CS), CORD, LIMBAR (LC), DEBRING (BC), INCREMINE (BC), INCREMINE (BC), LN, DTHER (CM), LONG (LU), MAMMARY GLAND (MG), MAD SAL (NAY GL (SG), MARRIA (SC), MARRIA (SG), MARRIA (SG), MARRIA (SG), MARRIA (SG), MARRIA (SG), STERNIM (SE),

SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, GL (ST), THYMUS (TH), THYROID (TY),

TRACHEA (TR), URINARY BLADDER (UB), UTFRUS (UT), ACOLLECTED/TAKEN (SM)

INFILTRATION, LYMPHOID, - SLIGHT

-PELUIS, DILAIATION,-MONFRATE -PFRTHRIBITHTALZPERTUASITHTAR

CUNG CLU

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: LIVER (LI)

^{***} ALL ORGANSZIJSSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOBLE) LARE SAUFD ***

APPENDIX B *** PATH/TOX SYSTEM OUTPUT *** SHBCHRONIC TOXICITY STUDY IN RAIS

PRINTED: 12-MAY-88 PASE: 331

STHDY NIMBER: 2399103

INDIVIDIJAL ANIMAL SIJMMARY REPORT

436 16/86 ECROPSY: 07/ NOT REQUIRED	реятн	WEEK OARA DAY	SCHE TERM	SCHEDULED, TERMINAL SACRIFICE TERMINAL BODY WEIGHT: 257.5 GRAMS RECORDER: SID JONES, DUM, PHD, DACUP WEIGHER: BARRARA DAY
ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO RODY WEIGHT (%)	ORGAN TO BRAIN METCHT RATIO	ORGAN STATUS
ADRENAL (AD)	. 063	2 PACT.	. 0317	LETCHT TAKEN
DUARY (DV)	. 087	.0338 %	. 0437	1
BRAIN W/STEM (BR)	1.99	. 273 %	1 . HO G	LIFT SHT TAKEN
HEART (HT)	.78	% £0£.	.392	WEIGHT TAKEN
SPLEEN (SP)	. 52	.202 %	.261	METCHT TAKEN
KIDNEY (KD)	1.78	.691 %	.894	METGHT TAKEN
LIVER (LI)	7.25	2.816 %	3.643	METGHT TAKEN
CLINICAL OBSERVATIONS	PATHOL	THOLOGY OBSERUATIONS NECROPSY		HISTOPATHOLOGY
-APPEARED NORMAL	GENERAL INFI	GENERAL INFORMATION (XX): >NOTE:>EXTERNAL GRISERUALIONES:MORE	LUNG (LU) : -PFRIGRENCH INFILTRATII	NG (LD): -PERIMENCHIAL/PERIMASCH AR, INFILTRATION, LYMPHOID,-SHIGHT

!

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AD), BUNE, FEMUR (SE), BONE, STERBUM (SB), BRAIN WYSTEM (BR), CECUM (CE), COLON (CO), CORO, CERVICAL (CS), CORO, LUMBAR (LC), CORO, THURACIC (TC), DUDDENUM (OU), ESOPHAGUS (ES), EYE (EY), HEART (HI), ILFIM (IL), JEININUM (JE), KIONEY (KD), FACRIMAL GL, FXO (FD), LIVER (LI), LN, MESENTERIC (MS), LN, DIHER (LN), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GL (SR), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), MFRUE, SCIATIC (SN), FWARY (MV), PAMMRES (PA), PARMHARY (PI), RECTUM (RE), SKIN (SK), SKIN, DIHER (SS), SPLEEN (SP), STOMACH, GL (ST), SIOMACH, NONGL (SU), IHYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (1B), HIFLELS (HI), AMMIERIT DATACH (MA) THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: KIDNEY (KD), LIVER (LI)

^{***} ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED OFR THE STUDY PROTOCOL) LAFOR SAULD ***

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/IDX SYSTEM DUTPUT *** APPENDIX R

PRINTED: 12-MAY-88 PAGE: 332

STHEY REFERENCE 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE STUDY WEEK OF DEATH: 14 PROSECTOR: TIM GROUE DOSE GROUP: 2 SEX: FEMALE DOS STUDY DAY OF DEATH: 96 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL DATE OF DEATH: 02/15/86 STUDY DAY OF OF DATE AND TIME OF NECROPSY: 02/15/86 12:15 ANIMAL NUMBER: B08437

TERMINAL BODY WEIGHT: 243,2 GRAMS RETAINFR: SID JOHES, DUM, PHD, DACUP

PATHOLDGIST: SID JONES, DUM, PHD, DACUP

WEIGHER: NOT REQUIRED BY PRINTOCK

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

	PATHOLOGY OBSERVATIONS	
CLINICAL OBSERVATIONS	NECROPSY	HISTOPATHOLOGY
-APPEARED NORMAL	COLLECTED/TAKEN (XW): -ELECTRON MICROSCOPY SAMPLE; LIUFR GENERAL INFORMATION (XX): >HOTE:>EXTERNAL OBSERVATIONS:NOWE:	KIDNEY (KD): -PELUES, DB ATATION,-SLIGHT LIVER (LI): -FELUE (LI): -FELUE (LI): -FERIEMBERTAL/PERIOSCHER, -NERIEMBERTAL/PERIOSCHER,
		1

ADRENAL, CORTEX (AC), ADRENAL, MEDILLA (AM), ADRIA, THORACIC (AD), ROME, FEMIR (FE), BONE, STERNIM (SB),
BRAIN WASTEM (BR), CECUM (CE), COLON (CD), CORO, CERVICAL (CS), CORD, LUMBAR (LC), CORO, THURACIC (TC),
BUDDENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILFIM (II), JEINRIM (JE), KIDNEY (KD), LAGRIMAR (S),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MS), MAND SALIVARY GL (SS),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERUE, SCIATIC (SN), DVARY (DV), PARTREAS (PA), PARATRYRUD (FI),
PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMMACH, GL (ST), STOMMAH, NDNAL (SU),
THYMUS (TH), THYROID (TY), TRACHEA (TR), UR)HARY BLADDER (1R), HTERIS (11) THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED FER THE STHOY FROTHEIN) WFRE SAUED ***

APPENDIX 8 *** PATH/IDX SYSTEM DUTPIN *** SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-86 PAGE: 333

INDIVIDUAL ANIMAL SUMMARY KEPURT

STHEY NIMBER: 2399108

TERMINAL BODY WEIGHT: 222.4 GRAMS
RECORDER: SIO JONES, DUM, PHD, DACUP
WEIGHER: NOT REQUIRED BY PROTOCOL SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE PATHOLOGIST: SID JONES, DUM, PHO, DAILUP STUDY WEEK OF DEATH: 14 PROSECTOR: DOUGLAS HERNOON DOSE GROUP: 2 DEATH: 97 STUDY DAY OF PIJST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL 9:12 SEX: FEMALE AND TIME OF NECROPSY: 07/16/86 DATE OF DEATH: 07/16/86 ANIMAL NUMBER: 808438

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

CLINICAL OBSERVATIONS

-APPEARED NORMAL

PATHOLOGY OBSERUATIONS
NECROPSY

*COLLECTED/TAKEN (XW) :
-ELECTRIN MICROSCUPY SAMPLE; LIVER
GENERAL INFORMATION (XX) :
>NOTE; EXTERNAL OBSFRUATIONS; MONE

FOCT OF MONOMUCLEAR CELLS, -SI ISHT LUNS (LT):
-PERTERCHIALA / PERTUASCH AR, INFILIRATION, LYMPHOTO, -SLIGHT

-WEPHENPAINY, CHRINIC PROBLESSIVE,-

KIDNEY (KD) -NEPHROPATI MINIMAL LIUER CLD :

HISTIJPATHII OGY

THE FOLLOWING ORGANS WERE LINREMARKABLE AT NECROPSY:

AORENAL, CORTEX (AC), ADRENAL, MEDILLA (AM), ADRITA, THORACIC (AD), BONE, FEMUR (FE), BONE, STERNIM (SB),
AORENAL, CORTEX (AC), ADRENAL, MEDILLA (CO), CIRO, CIRO, CIRO, LIMBAR (LC), CORD), THERACIC (TE),
BODDENIM LOSTEM (BR), CECUM (CE), COO, CIRO, CERUICAL (CS), CIRO, CIRO, LIMBAR (LO), KIDNEY (KO), LACRIMAL GL, EXO (CE),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LIMB (LI), MARMARRY (GV), PANCREAS (PA), PARATHYROID (PT),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), OWARY (GV), PANCREAS (PA), PARATHYROID (PT),
PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPLEN (SP), STEMMEH, SI (ST), STEMMEH, NOWSI (SI),
THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UR), UTERUS (UT)

*** ALL ORGANS/TISSUES (REQUIRED TO BE MARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/TOX SYSTEM OUTPUT *** APPENDIX 8

PRINTED: 12-MAY-80

INDIVIDUAL ANIMAL SIMMARY REPORT

STUDY NUMBER: 2399308

SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE	STLIDY WEEK OF DEATH: 14 TERMINAL BRIDY WEIGHT: 261.4 GK	DAY: RECORDER SID JOHES, DUM, PH	PATHOLOGIST: SID JONES, DUM, PHD, DAMUP WEIGHER: NOT REQUIRED BY PRO	
DOSE GROUP: 2	DEATH: 97 STUDY WEE	PRINSECTOR: BARBARA DAY	PATHOLOGIST: SID JOH	
SEX: FEMALE	STUDY DAY OF DEATH: 97	07/16/86 10:50	IREO BY PROTOCOL	
ANIMAL NUMBER: 808439	DATE OF DEATH: 07/16/86	DATE AND TIME OF NECROPSY: 07/16/86 10:50	POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL	

PHD, DACUP **ELECTION** RAMS

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

	PATHOLOGY OBSERUATIONS	
CLINICAL DBSERVATIONS	NECROPSY	HISTOPATHOLOGY
		244522122222222222222222222222222222222
-APPEARED NORMAL	^COLLECTED/TAKEN (XW) :	LUNG (L.U) :
	-ELECTRON MICROSCOPY SAMPLE; LIVER	-PERTERMENTAL ZPERTUASION AR,
	GENERAL INFORMATION (XX):	INFILTRATION, LYMPHOID, -SI IGHT
	>NOTE:>FXTERNAL DBSFRUATIONS:NOTE	
		1

DUDDENUM, CORTEX CECUM CED, COLON (CD), GIRD, LIMBAR (LE), BIDNE, STERNIM (SB),
BRAIN WASTEM (BR), CECUM CED, COLON (CD), CIRD, CERVICAL (CS), CIRD, LIMBAR (LE), CIRD), THIRACLE (TC),
BRAIN WASTEM (BR), CECUM CE), EYE (EY), HEART (HT), ILEUM (IL), JEJUNIM (JE), KIDNEY (KD), LACRIMAL GI, EXD (ED),
DUDDENUM (DU), ESDPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNIM (JE), MONEY (KD), LACRIMAL GI, LN, CIRD, CH), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), QUARY (DU), PANCREAS (PA), PARATHYRNID (PT),
PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN (SK), DRINARY BLADDER (UB), UTERUS (UT) FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY: 포

FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: KIDNEY (KD), LIVER (LI) 포

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY FRITHIND) WERE SAUFD ***

APPENDIX 8 *** PATH/IOX SYSTEM OUTPUT *** SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-may-88 PAGE: 335

STHEY NUMBER: 9399188

INDIVIDUAL ANIMAL SIMMARY REPORT

ANIMAL NUMBER: B08440 SEX: FEMALE DATE OF DEATH: 07/16/86 STUDY DAY OF DATE AND TIME OF NECROPSY: 07/16/86 14:38 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL	ОЕАТН	U 22: U7	SCHF TERM	ECHIDALED, TERMINAL SACRIETCE TERMINAL BIDY WEIGHT: 253.9 GRAMS RECORDER: SJD JONES, DVM, PHD, DACUP WEIGHER: DOUGLAS HERNOOM	CUP
ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (*)	ORGAN TO BRAIN METGHT RATIO	ORGANSIALUS	\$1. TV
ADREFIAL (AD)	.076	. 18298 % . 18298 %	. 0618	WE 13HT TAKEN	
BRAIN W/STEM (BR)	1.96	.338 %	1.000	WEIGHT TAKEN	
SPLEEN (SP) KIDNEY (KD)	.60	.238 % .719 %	933	WEIGHT TAKEN	
LIVER (L1)	8.115	3.169 %	4.11?	UFIGHT TAKEN	i i t
CLINICAL OBSERVATIONS	α	THOLOGY OBSERUATIONS NECROPSY	SNO	HISTOPATHOLOGY	, i
-APPEARED NORMAL	GENERAL INFO	GENERAL INFORMATION (XX): >NOTE:>FXTERMAL (RISERVATIONES:MONE	LUNG (LIB) ; -PERBEREH INFILTRATI	NG (LID): -PERIMENHAL/PERIMASCIMAR, INFILTRATION, LYMPHOID,-SI (GHT	

ADRENAL, CORTEX (AC), ADRENAL, MEDITLA (AM), ATRIA, THORACIC (AU), BUNE, FFMIR (FF), BUNE, SIFRNIM (SB),
BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
BUNDOENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HI), IFNIM (LE), SEDINEY (KD), ACRIMAL A, FXM (FM),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MS), MAND SALIVARY GI (SG),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), (WARY (MU), PANCKERS (PA), PARCHER (SM),
PITULIARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMMOH, GL (ST), STOMMOH, NOMBEL (SD),
THYMUS (TH), THYROLD (TY), TRACHEA (TR), LRIMARY BLADDER (18), HTERIS (11), ASTHEEN (SM) THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: KIDNEY (KD); LIVER (LI)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAUFD ***

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/TOX SYSTEM DITIPUT *** APPENDIX B

PRIMITED: 12-MAY- 98 PAISE: 736

STEEP NUMBER: 2399108

INDIVIDIDAL ANIMAL SLIMMARY REPORT

ANIMAL NUMBER: 808441 SEX: FEMALE DATE OF DEATH: 07/16/86 STUDY DAY OF DATE AND TIME OF NECROPSY: 07/16/86 15:06 POST-FIX WEIGHER: NOT REGUIRED BY PROTOCOL	DEATH	DOSE GROUP: 2 SACRIFICE STATUS: 97 STUDY WEEK OF DEATH: 14 PROSECTOR: TIM GROUE PATHOLOGIST: SID JONES, DUM, PHD, DACUP	SCHE TERM	SCHFONFO, TERMINAL SACRIFICE TERMINAL BODY WFIGHT: 254.6 GRAMS RECORDER: SIO JUNES, OUM, PHO, DACUP WEIGHER: TIM GROVE
A CIRGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO RODY WEIGHT (%)	ORSAN TO BRAIN LEIGHT RATIO	ORGAN
ADRENAL (AD)		\$ CUAD.	1620.	METCHT TAKEN
DVARY (DV)	.108	.0424 %	.0551	METGHT TAKEN
BRAIN W/STEM (BR)	1.96	2 077.	1.000	UFIGHT TAKEN
HEART (HT)	.89	. JUST 10 %	. 45.4	MEIGHT TAKEN
SPLEEN (SP)	.40	.157 %	286.	MF ICHT TAKEN
KIONEY (KD)	1.88	.738 %	656.	METGHT TAKEN
LIVER (LI)	8.50	3.339 %	4.337	LETCHT TAKEN
,	JOHLES	THOLDGY ORSERUATIONS	0.8.5	9 7 7 7 7 7 7 7 7 9 9 5 5 5 5 5 5 5 5 6 6 6 7 7 7 7 7 7 7 7 7
CLINICAL DBSERUATIONS		NECROPSY		HISTOPATHOLOGY
-APPEARED NORMAL	: 45 : 5 : 1 : 1 : 1	GENERAL INFORMATION (XX):	LIVER OLD :	VER (LD:

DUDDENIM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HI), ILEUM (IL), JEJÚNIM (JF), KIĎNEY (KD), LACRIMAL GL, EXD (ED), LIVER (LI), LN, MESENTERIC (MS), LN, DTHER (LN), LING (LH), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERUE, SCIATIC (SN), DVARY (DV), PANCREAS (PA), PARATHYRHO (PT), PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, DIHER (SS), SPLFFH (SP), SHIMACH, BL (SD), SHIMACH, BL (SD), SHIMACH, BL (SD), THYROLD (TY), TRACHEA (TR), URINARY BLADDER (UR), UTERUS (UT), ACOLLECTED/TAKEN (XD) THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:
ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRIA, THORACIC (AD), BONE, FEMUR (FE), BONE, STERNUM (SR),
BRAIN W/STEM (BR), CECUM (CE), COLON (CD), CORD, CRVITCAL (CS), CORD, LURBAR (LD), FEMORE (LD),
BRAIN W/STEM (BR), CECUM (CE), COLON (CD), CORD, CRVITCAL (CS), CORD, LURBAR (LD), CORD, COLON (CD), COLON (CD), CORD, COLON (CD), CORD, COLON (CD), CORD, COLON (CD), COLON (CD), CORD, COLON (CD), CORD, COLON (CD), CORD, COLON (CD), CORD, COLON (CD), COLON (CD), CORD, COLON (CD), COLON (CD), COLON (CD), CORD, COLON (CD),
INFILTRATION, LYMPHOID, - SLUGHT

- PERTERMENTHIN ZPFRIUASMI AR

LUMBS (LU):

FOLLOWING TISSUES WERE UMREMARKABLE AT MICROSCOPIC EXAMINATION: KIDNEY (KD)

^{***} ALL ORGANSZTISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCHIO LIFTE SAULD ***

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/IOX SYSTEM DUIPUT *** APPENDIX B

PRINTED: 12-MAY-8/ PAILE: 337

INDIUTORIAL ANIMAL SIMMARY REPURT

STUDY NEWFER 9399108

TERMINAL BODY WEIGHT: 247.8 GRAMS RECORDER: SID JONES, DUM, PMD, DACUP SACRIFICE STATUS: SCHEDNIED, TERMINAL SACRIFICE PATHOLOGIST: SID JONES, DUM, PHD, DACUP STUDY WEEK OF DEATH: 14 PROSECTOR: BARBARA DAY DOSE GROUP: 3 DEATH: 95 STUDY DAY OF POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL AND TIME OF NECROPSY: 07/14/86 10:29 SEX: FEMALE DATE OF DEATH: 07/14/86 ANIMAL NUMBER: 808462

METGHER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

CLINICAL DBSERVATIONS

-APPEARED NORMAL

PATHOLOGY OBSERVATIONS NECROPSY

↑COLLECTED/IAKEN (XW) :
-ELECTRIN MICROSCOPY SAMPLE; LIUFR GENERAL INFORMATION (XX) :

>NOTE:>EXTERNAL OBSERVATIONS: MONE i

INFILTRATION, LYMPHOID, -SLIGHI

- PERTORINATION / PERTONS SITE AR

: (CT) :

HISTOPATHOLOGY

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRTA, THORACIC (AD), BINE, FEMUR (FE), BONE, STERNIM (SR), BRAIN MASTEM (BR), CECUM (CE), CHO, CRUD, CECUM (CE), CHO, CRUD, CECUM (CE), CHO, CRUDENUM (JE), KIONEY (KD), LACRIMA GL, EXO (ED), DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIONEY (KD), LACRIMA GL, EXO (ED), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LU), MAMMARY GLAND (MS), MAND SALVOARY GLOS, MAND SALVOARY GLOS, MAND SALVOARY GLOS, PARATHYRUID (PT), PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPICEN (SP), STIMACH, GLOS), STICMACH, GLOS), TRACHEA (TR), URINARY BLADDER (UH), UTERUS (UT) THE FOLLOWING ORGANS WERE INREMARKABLE AT NECRUPSY:

FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC FXAMINATION: KIDNEY (KD), LIVER (LI) *** ALL DRSANS/TISSUES (REQUIRED TO BE HARVESTED FER THE STRIDY PROTOBLE) WERE SAUFD ***

APPENDIX 8 *** PATH/INX SYSTEM DEITFUR *** SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88

STHDY NIMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

TERMINAL BODY WEIGHT: 236.6 GRAMS RECORDER: SID JAMES, DUM, PUD, DAEUP SACRIFICE STATUS: SCHEDMED, TERMINAL SACRIFICE WEIGHER: BARBARA DAY PROSECTOR: PARBARA DAY PATHOLOGIST: SID JONES, DUM, PHD, DACUP STUDY WEEK OF DEATH: 14 DASE GROUP: 3 STUDY. DAY OF DEATH: 95 POST-FIX WEIGHER: NOT REGUIRED BY PROTOCOL DATE OF DEATH: 02/14/86 STUDY.DAY OF DATE AND TIME OF NECROPSY: 02/14/86 10:09 SEX: FEMALE ANIMAL NUMBER: B08463

		11111111111111111111		* * * * * * * * * * * * * * * * * * * *	†
	ABSOLUTE ORGAN WEIGHT	ORGAN WEIGHT RELATIVE	ORGAN TO BRAIN	ORSAN	
ORGAN NAME	(GRAMS)	10 BODY WEIGHT (%)	MEIGHT RATIO	STATUS	
	1 1 1 1 1	1 1 1 1 1 1 1			
ADRENAL (AD)	.075	2 N 3 1 2 1 2 1 2 1 2 1 2 1 2 1 2 1 2 1 2 1	. 0383	METSHT TAKEN	
DUARY (DU)	.116	.0489 ₺	.0591	WEIGHT TAKEN	
BRAIN W/STEM (BR)	1.96	8 2 2 8 3 Y	1.000	WEIGHT TAKEN	
HEART (HT)	08.	.338 %	. 408	METGHT TAKEN	
SPLEEN (SP)	. 55	23.4 18	E SS.	WFIGHT TAKEN	
KIDNEY (KD)	1.73	733 K	.886	METGHT TAKEN	
LIVER (LI)	8,95	3, 283 %	4.574	LETCHT TAKEN	
	10HLEd	ATHOLOGY ORSERUATIONS	0 × 0	11111111111	1
CLINICAL OBSERUATIONS		NECROPSY		HISTOPATHOLOGY	
-APPEARED NORMAL	GENERAL INFOR	GENERAL INFORMATION (XX): >NOTE:>EXTERNAL DBSFRUALIONS:NONF	LUNG (LD) : - PER HARINCH INFILTRATIO	NG (LU): -PERPERINCHIAL/PERIVASCULAR; INFILTRATION, LYMPHOID,-SI IGHT	t L

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL AT NECOPSY:

ADRENAL, CORTEX (AC), ADRENAL MEDULLA (AM), AGRIA, THORACIC (AC), EIRB, (FF), EIRB (FF), EIRB (TC),

BROAIN W/STEM (BR), CECUM (CO), CORO, CERVICAL (CS), CORO, LIMBAR (LC), EIRB, THOREY (ED),

BUODENUM (DI), ESOPHAGUS (ES), EYE (EY), HEART (HI), ILEM (II), JEJINSH (E), KIDNEY (E), LACRIMA (E),

ELUGE (L), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG), MAND SALIUARY GL (SR),

MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NFRUE, SCIATIC (SN), MUACHER (FO), FARITHERS (FA), FARRATHYRHID (PI),

FITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, MINNEL (SD),

THYMUS (TH), THYRGID (TY), TRACHER (TR), LIRIMARY BLADDER (TR), LIFRIS (TI), ACRES (FEED)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: KIDNEY (KD), LIVER (LI)

*** ALL ORGANSTISSUES (REQUIRED TO BE HARVESTED PER THE STIMY PRITITION WHRE SAULD ***

*** PATHATOX SYSTEM OUTPUT *** SUBCHRONIC TOXICITY STIDY IN RAIS APPEND1X_8

PRINTED: 12-MAY-88

STUDY NIMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: B08464 SEX: FEMALE DATE OF DEATH: 07/14/86 STUDY DAY OF DATE AND TIME OF NECROPSY: 07/14/86 13:37 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL	ОЕАТН	DOSE GROUP: 3 SACRIFICE STATUS: 95 STUDY WEEK OF DEATH: 14 PROSECTOR: BARBARA DAY PATHOLOGIST: SID JOHES, DUM, PHD, DAILUP	SCHE	SCHEDULED, TERMINAL SADRIFICE TERMINAL BODY WEIGHT: 239.5 BRAMS RECORDER: SID JUNES, DUM, PHO, DADUP WEIGHUR: RARRARA DAY
ORGAN NAME	ABSOLITE ORGAN METGHT (GRAMS)	DRGAN WEIGHT RECATIVE TO BODY WEIGHT (%)	DRIGHT OF PROTE WEIGHT RATIO	ORGAN STATUS
ADRENAL (AD) CUARY (CU) BRAIN W/STEM (BR) HEART (HT)	. 069 . 116 1.98	. 0287 % % 828 % % % % % % % % % % % % % % % %	.0347 .0584 1.000	METGHT TAKEN METGHT TAKEN WETGHT TAKEN WETGHT TAKEN
SPLEEN (SP) KIDNEY (KD) LIUER (LI)	.39 1.78 7.95	.161 % .743 % 3.320 %	.195 .897 4.011	METGHT TAKEN METGHT TAKEN METGHT TAKEN
CLINICAL OBSERVATIONS	Œ.	THOLOGY OBSERUATIONS NECROPSY	S N O	RISTAPATION TASY
-APPEARED NORMAL	GENERAL INFI	GENERAL INFORMATION (XX): >NOTE:>EXTERNAL OBSERVATIONS:NONE	- PERIBRINCH - PERIBRINCH - PERIBRILIAN	NS ((()) (-PERIBRANCHIAL/PERIVASCHIAR, INFNI IRATION, PYMPHAIO,-SLIGHI

FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ATMITA, THORACIC (AD), SOBE, FEMIR (FF), ROBE, STERBIN (SR),

BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORO, CERVICAL (CS), CORO, LUMBAR (LC), CORO, THORACIC (TC),

BRAIN WASTEM (BR), CECUM (CE), EYE (EY), HEART (HT), ILEUM (HI), NEURING (HS), KIONEY (KO), LACREMAN (H),

LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLANO (MS), MAND SALIVARY GL (SS),

MARROW, STERNUM (SE), MISCLE, SKELFTAL (SM), NERUE, SCIATIC (SH), OWARY (HU), PANCREAS (PA), PARALHYRID (FI),

PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPIER (SP), STOMACH, GL (ST), STOMACH, KE)

THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (HB), HTRRIS (HI), ACORTECTOR (KM)

포

FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: KIDNEY (KD), LIVER (LI) 포

^{***} ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTECTED WERE SAULD ***

APPENDIX 8 *** PATHZIDX SYSTEM DUIPUT *** SUBCHRONIC TOXICITY STUDY IN RATS

FRINTED: 12-MAY-86 PAGE: 340

STUDY NUMBER: 2399100

INDIVIDUAL ANIMAL SUMMARY REPORT

RECORDER: SID JUNES, DUM, PUD, DACUP INFILTRATION, LYMPHOID, -MINIMA 249.3 GRAMS LIFT SHIT TAKEN TAKEN UF IGHT TAKEN WFIGHT TAKEN TEKFM TAKEN TOKEN 31 4 4 1 3 0 R G A N - PERTERCHICHTAL / PERTUASIBLAR HISTOPATHOLOGY SACRIFICE STATUS: SCHEDWIFD, TERMINAL SACRIFICE ME IGHT THE FIGURE LE EGHT F 15H1 -DILATATION, -SI. IGHT TERMINAL BODY WFIGHT: WEIGHER: TIM GRIDUE HEREN CEED .. : (ICD 9401 ORSAN TO BRAIN METCHT RATIO .0668 .8287 1,8110 . 421 .063 1.135 O B S E R U A T 1 O N S PATHOLOGIST: SID JONES, DUM, PHD, DAISUP STUDY WEEK OF DEATH: 14 ORGAN WEIGHT RELATIVE -LIMEN, FLIID; BOTH HORRS, CLEAR >NOTE:>EXTERNAL ORSERVATIONS:NOME TO BRIDY METCHT (%) . 11717 .0505 .858 .318 95. .201 2,429 GENERAL INFORMATION (XX) : NECROPSY PROSECTOR: TIM GROUE DOSE GROUP: 3 PATHOLOGY UTERUS (UT): ABSOLUTE ORGAN WEIGHT STIJDY DAY OF DEATH: 95 (GRAMS) . 054 .126 2.14 6.N5 1.98 .79 5.0 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL SEX: FEMALE DATE AND TIME OF NECROPSY: 07/14/86 13:58 CLINICAL DRSERVATIONS (BR) DATE OF DEATH: 07/14/86 ANIMAL NUMBER: B08465 BRAIN W/STEM 9 ŝ (SP) 9 Œ (1) DRIGHN NAME - APPEARED NORMAL ADRENAL SPLEEN DUARY K 1 DNEY HEART LIVER

ADRENAL, CORTEX (AC), ADRENAL, MEDILLA (AM), ANRIA, THURACIC (AN), ROWE, FEMUR (FF), MANE, STERMUM CED), BRAIN WZSTEM (BR), CECUM (CE), COLON (CO), CARD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THURACIC (TN), DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILFUM (LL), JEAUNUM (DE), KIDNEY (KD), LAGRIMAL GI), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MS), MAND SALIVARY GL (SR), MARROW, STERNUM (SE), MISCLE, SKELETAL (SM), NERUE, SCIATIC (SN), DVARY (NV), PARTRESS (PA), PARATRYRHID (PT), PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NOWAL (SD), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY PLADGER (NR), ACHIEFIEDZIAREN (XW) THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: KIDNEY (KD), LIVER (LI)

^{***} ALL ORGANS/TISSUES (REQUIRED TO BE HARUESTED PER THE STADY PROTOTO) WERE SAULD ***

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/TRX SYSTFM OHIPHIT *** APPENDIX 8

PRINTED: 12-MAY-80 PAGE: 341

INDIVIDIDAL ANIMAL SHMMARY REPORT

STUDY NUMBER: 9399188

TERMINAL BODY WFIGHT: 26 RECREDER: BARBARA DAY SACRIFICE STATUS: INSCHEDULED (D) PATHOLOGIST: NOT RECAUTRED BY PROTOCOL 4: 88 STUDY WEEK OF DEATH: 13 PRESECTOR: RARBARA DAY DOSE GROUP: 3 STUDY DAY OF DEATH: 88 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL SEX: FEMALE DATE AND TIME OF NECROPSY: 07/07/86 14:58 ANIMAL NUMBER: 808466 DATE OF DEATH: 07/07/86

WEIGHER: NOT REGIJIRED BY PROTOCO!

HISTOPATHOL DISY

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

-APPEARED NORMAL

INFILTRATION, LYMPHOID, -SI IGHT PFRIRETHERM MINISTER OFFICE CONTRACTOR -FORETCH MATERIAL, -PRESENT CUNG CLID : PATHOLOGY OBSERVATIONS -MOTTLED; ALL LOBES, LIGHT TO DARK RED OBSERVATIONS: NONE, FOUND DEAD AT ONE HOUR POST-DOSE OBSERVATIONS -FAILURE TO COLLAPSE; ALL LURES NOTE: JLAST IN-LIFE AND EXTERNAL GENERAL INFORMATION (XX) : NECROPSY = CLINICAL OBSERVATIONS

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDILLA (AM), AGRIA, THORACIC (AG), EDINE, FEMIRE, FEMIRE, STERNIM (SB),

BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORO, CERVICAL (CE), CORO, THORACIC (TC),

BRAIN WASTEM (BR), CECUM (CE), HEART (HT), ILFIM (IL), JFJINTH (JF), KIDNEY (KD), LAGRIMAL GI, EXO (ED),

DUDDENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILFIM (MS), MAND SALIVARY GI, MARROLL, STERNIM (SF),

LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), MARMARY (GD), PARCHERS (PA), PARATHYROID (FT), FILTITIARY (FI), RECTIM (RF),

MISCLE, SKELETAL (SM), NEVUE (SP), STOMACH, GL (ST), STOMACH, NINISL (SU), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (HB), HIFRUS (HI), ACMLLECTED/TAKEN (XW)

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AN), AURTA, THURACIC (AU), BUBE, FFMIR (FE), BIRDE, STERNUM (UR),
BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LIMBAR (LC), CORD, THURACIC (TC),
BUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HFARI (HI), ILFUM (IL), KIDMEY (KD), LATRIMAL BI, FXD (FD),
LIUER (LI), LN, MESENTERIC (MS), MAMMARY GLAND (MS), MAND SALIUARY GI (SG), MARROW, STERNUM (SF), MISCLE, SKFLFTAI (SN),
NERUE, SCIATIC (SN), OUGRY (DU), PANICREAS (PA), PARROY (PI), PITHIDARY (PI), RETUM (RF), SAIN (SK),
SPLEEN (SP), STOMACH, GL (SI), STOMACH, NONSL (SID), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BIADDER (18), FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: UTERUS (UT) HH

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STRINY PRITOCH) LISTE SAUCH ***

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/TOX SYSTEM DITIPUT *** APPENDIX 8

PRINTFD: 12-MAY-88 PAGE: 342

INDIVIDUAL ANIMAL SUMMARY REPURT

STIES MERFE: 2399108

TERMINAL BODY METGHT: 257.2 GRAMS RECREDER: SID JONES, DUM, PHD, DACUP SACRIFICE STATUS: SCHEDULED, FEMILIAL SACRIFICE PATHOLDGIST: SID JONES, DVM, PHD, DACUP STUDY WEEK OF DEATH: 14 PRINSECTOR: BARRARA DAY DOSE GROUP: 3 DEATH: 95 STLIDY DAY OF POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL SEX: FEMALE DATE AND TIME OF NECROPSY: 07/14/86 11:29 ANIMAL NUMBER: B08467 DATE OF DEATH: 07/14/86

WELIGHER: NOT REQUIRED BY PRINTING

*** ANIMAL HAS NO DRGAN WEIGHTS RECORDED ***

PATHOLOGY OBSERVATIONS CLINICAL DBSERVATIONS

-APPEARED NORMAL

-ELECTRIN MICROSCOPY SAMPLE; LIUFR GENERAL INFORMATION (XX) COLLECTED/TAKEN (XW) :

NECROPSY

VIOTE: VEXTERNAL DRSERVATIONS: NOVE

INFILTRATION, LYMPHOID, -SI IGHT -PERTBRONCHIAL / PERTUASION AR.

(B'C SMIT MINIMAL

-NEPHRIPATHY, CHRONIC PROGRESSIUS,-

KIDNEY (KD)

HISTOPATHIN DISY

ADRENAL, CORTEX (AC), ADREMAL, MEDULLA (AM), ANOTA, THORACIC (AN), BINE, FEMIR (FF), BOWE, SIERBIM (SB), BORENAL, CORD, COCO, CORO, CORO, CORO, CORO, THORACIC (TC), BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORO, CERVICAL (CE), CORO, LUMBAR (LC), CORO, LUMBAR (CE), KIDNEY (KD), LASENTERIC (MS), LA, OTHER (LN), LUMG (LU), MAMMARY GLAND (MG), MAND SALIVARY GL (SS), MASCLE, SKELETAL (SM), HENUE, SCIATIC (SN), QUARY (NU), PANSTEAS (PA), PARSTEAS (PA), PARSTEAS (PA), PARSTEAS (PA), PARSTEAS (PA), THYROLD (FT), THYMUS (TH), THYROLD (TY), TRACHEA (TR), URINARY BLADDER (LR), HIFRUS (HI) THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: LIVER (L1) Ξ

ALL DRGANS/TISSUES (REDUIRED TO BE HARVESTED PER THE STIMY PRITIGIAL) WERE SAVED ***

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/TOX SYSTEM NITPHIT *** APPENDIX 8

PRINTFD: 12-MAY-88 PAGE: 343

INDIVIDIDAL ANIMAL SUMMARY REPURT

STUDY MIMBERS 2399108

201.3 GRAMS TERMINAL BODY WEIGHT: 21 SAIRLETTE STATUS: HISTORDHIED (D) PATHOLOGIST: NOT REQUIRED BY PROTOCOL 4: 18 STUDY WEEK OF DEATH: 3 PROSECTOR: BARBARA DAY DOSE GROUP: 3 DEATH: 18 STUDY DAY OF POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL AND TIME OF NECROPSY: 04/28/86 15:33 DATE OF DEATH: 04/28/86 ANIMAL MUMBER: B08468

WEIGHER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

CLINICAL DBSERVATIONS

PATHOLOGY OBSERVATIONS NECROPSY

-MOTTLED; ALL LORES, LIGHT TO DARK RED -FAILURE 10 COLLAPSE; ALL LIPES .. 0x3 GENERAL INFORMATION LUNG (LU) :

INFILIRATION, LYMPHOID, -SLIGHT -PERTERMENTAL APERTUASION OR - FIRE ISN MATERIAL, - PRESENT

FUNG (LLI) :

HISTOPATHOLOGY

CHSFRUATIONS:NOWE. DIED WITHIN >NOTE:>LAST IN-LIFE AND EXTERNAL ONE HOUR OF DOSING

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NETROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AURTA, THORACIC (AD), BINE, FEMUR (FE), BONE, STERNUM (SR),
BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORD, CHAND, LIMBAR (LC), CHRD, LACRIMAL GL, EXO (EO),
DUDDENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJINUM (JE), KIDNEY (KD), LACRIMAL GL, EXO (EO),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), MAMMARY GLAMO (MG), MAND SALVORY GL (SR), MARKKIL, STERNUM (SF),
MUSCLE, SKELETAL (SM), NERUE, SCIATIC (SN), DUARY (OU), PANCREAS (PA), PARATHYROID (PT), PITHITARY (PI), RECTUM (RE),
SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, GL (ST), THYRUS (TH), T

ADRENAL, CORTEX (AC), ADRENAL, MEDILLA (AN), ADRIA, THURACIC (AD), BUNE, FIRER (FE), SURE, SIFRUEN (SE),
BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORD, CFRUICAL (CS), CORD, LUMBAR (LC), CORD, THURACIC (TC),
DUCDENUM (DU), ESOPHAGUS (ES), EYE (FY), HEART (HT), ILFIM (IE), AFLIBUEN (AF), KIDIRY (KD), LACRIMAN (SF), MUSTIE, SKELEFAL (SM),
LIVER (LI), LN, MESENTERIC (MS), MAMMARY GLAND (MS), MAND SALIVARY GL (SG), MARROLL, STERNIM (SF), MUSTIE, SKELEFAL (SM),
NERUE, SCIATIC (SN), OVARY (OV), PANCREAS (PA), PARATHYRIDD (PT), PITHITARY (PI), RETHEM (BE), SKIN (SA),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONSL (SU), THYMUS (TH), THYROLD (TY), TRACHEA (TR), URINARY BLADDER (IR), THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: JTERUS (UT)

*** ALL DRGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOROR) WHOR SAUFD ***

APPENDIX 8 *** PATH/INX SYSTEM DULPHIT *** SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88 PANE: 144

INDIVIDUAL ANIMAL SHMMARY REPURT

STIBY REMOTE: 2399108

TERMINAL BODY WEIGHT: 258.1 GRAMS REFINDER: SID ADNES, DUM, PHD, DACUP WEIGHER: NOT REQUIRED BY PRITORIN SACRIFICE SACRIFICE STATUS: SCHEDULED, TERMINAL PATHOLOGIST: SID JONES, DUM, PHD, DACUP STUDY WEEK OF DEATH: 14 PROSFERINRE TIM GREENE DASE GROWP: 3 STUDY DAY OF DEATH: 95 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL DATE AND TIME OF NECROPSY: 07/14/86 14:21 SEX: FEMALE DATE OF DEATH: 07/14/86 ANIMAL NUMBER: B08469

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

-NEPHROBARY, CHRONIC PROGRESSIVE,--FOCT OF MONONINGER CELLS, -MINIMA INFILIRATION, LYMPHOID, -SLIGHT -PERTHREMEDIAL APPRIORS OF AR HISTOPATHOLOGY FIUFF CLD : KIDNEY (KD) CONG COD: TIME IN IN OBSERUATIONS -ELECTRIN MICROSCOPY SAMPLE; LIUFR MANUTE: SEXTERNAL DRSERUATIONS: NORF GENERAL INFORMATION (XX) : NECROPSY ACOLLECTED/TAKEN (XW) PATHOLOGY THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY: CLINICAL DBSERVATIONS -APPEARED NORMAL

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ANTRA, THORACIC (AB), BONE, FEMUR (FE), BONE, STERNIM (SB),
BRAIN WASTEM (BR), CECUM (CE), DOLON (CD), CORD, CERVICAL (CS), CORD, LIMBAR (LC), CORD, SCOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEDUMUM (DE), KIDNEY (KD), LACRIMAL GL, EXD (EB),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LIMB (LD), MAMMARY GLAD (MS), MAND SALIVARY GLOSS,
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERUE, SCIATIC (SN), QUARY (DU), PANCREAS (PA), PARATHYROID (PC),
PITUTARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPLEN (SP), STUMMIH, RL (ST), STUMMIH, RICST), THYMOLO (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT)

*** ALE ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STIMY PROTOKON) MERE SAVED ***

APPENDIX 8 *** PATH/INX SYSTEM MUTPHT *** SUBCHRANIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-80 PAISE: 349

STIENY MIMPIER: 2399188

INDIVIDUAL ANIMAL SUMMARY REPORT

RECHROFER SID JOHES, DUM, PRID, DACENP 236.9 GRAMS TEKFN LIFTGHT TAKEN TAKEN TAKEN TAKEN TAKEN TAKEN 0 T T T L 0 -PERTURBUTHIAL / PERTUASITH AR 0 R G A N HISTOPATHOLOGY SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE ME IGHT THE LEH 1491 3M LF I H HILE LE LEHT WEIGHER: TIM SRIUF TERMINAL BODY WEIGHT: LUNG (LID) ORGAN TO BRAIN MEJIGHT RATIO . 6313 .0581 .418 .919 1.000 [\(\frac{1}{2} \) 3.475 PATHOLOGY OBSERUATIONS PATHOLOGIST: SID JONES, DUM, PHD, DACUP STUDY WEEK OF DEATH: 14 ORGAN WEIGHT RELATIVE ANDTE: VEXTERNAL DBSERVATIONS: NOVE TO BODY WEIGHT (%) .0457 . 0246 . 723 329 .260 2.733 GENERAL INFORMATION (XX) : NECROPSY PROSECTOR: FIM GROVE DASE GREHP: 3 ABSOLUTE ORGAN WEIGHT STUDY DAY OF DEATH: 96 (GRAMS) .108 050 . 78 1.71 6.47 62 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL 9:32 SEX: FEMALE DATE AND TIME OF NECROPSY: 07/15/86 CLINICAL OBSERVATIONS BRAIN W/STEM (BR) DATE OF DEATH: 07/15/86 ANIMAL NUMBER: B08470 (A) (SP) (X) E 9 <u>-</u> ORGAN NAME -APPEARED NORMAL ADRENAL SPLEEN K10NEY DUARY LIVER HEART

DUCTOR CONTEX (AC), ADRENAL, MEDILLA CAN), ANTRA, THORACIC CAD), BIRE, FFMIR (FF), BIRE, SIFREM (CE),

BRAIN MASTEM (BR), CECUM (CE), COLON (CO), CORD, CERUICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),

BRAIN MASTEM (BR), CECUM (CE), EYE (EY), HEART (HI), HEART (HI), LEGINEM (LE), KIDMEY (KO), LASPEMAL MA, FXO (FID),

LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MS), MAND SALIVARY GL (SS),

MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NENGE, SCIATIC (SN), ONARY (NO), PARGRES (PA), PARATHYROLD (FT),

PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, KND, MING (SD),

THYMUS (TH), THYROLD (TY), TRACHEA (TR), HRINARY BLADDER (LB), HTERIS (HI), ACHIECTED/JAKEN (XM) THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

INFILTRATION, LYMPHOID, -SLIGHT

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: KIDNEY (KD), LIVER (LI)

^{***} ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PFR THE STIDY PRITICIAL) WITH SAUFD ***

APPENDIX B *** PATH/INX SYSTEM MITPUT *** SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-RD PACE: 346

STUDY MIMBER: 9399108

INDIVIDUAL ANIMAI SUMMARY REPORT

RECEIRDER: SID JAINES, DUM, PHO, DAKUP 249.4 GRAMS METCHT TAKEN TAKFN TAKEN TAKEN TAKEN TAKEN TRKEN STATUS 2000 SACRIFICE STATUS: SCHEDULTD, TERMINAL SACRIFICE LIF I GHT LIF JOHT LIFT I GHT HE LEH UF LGHT LIFT FOLD WFIGHER: BARBARA DAY TERMINAL BRIDY MFIGHT: DRISAN TO BRAIN WEIGHT RATIO .0751 . 846.2 585 1.070 1.0310 3.66 5. 684 D B S E R U A T I D.N S PATHOLDGIST: SID JONES, DUM, PHD, DACUP STUDY WEEK OF DEATH: 14 ORGAN METGHT RELATIVE TO FINDY WEIGHT (%) 97.50 .0560 .377 .273 . 746 . 798 4.239 PROSECTOR: BARBARA DAY DOSE GROUP: 3 ATHOLOGY ABSOLUTE ORGAN WEIGHT STUDY DAY OF DEATH: 96 (GRAMS) . 086 .140 1.86 .94 69 1.99 10.57 POST-FIX WEIGHER: NOT REDUIRED BY PROTOCOL DATE AND TIME OF NECROPSY: 07/15/86 14:20 SEX: FEMALE DATE OF DEATH: 07/15/86 ANIMAL NUMBER: 808471 (A) W/STEM 8 (SP) 9 (H) <u>-</u>1 DRGAN NAME ADREMAL SPLEEN DUARY KIDNEY BRAIN HEART LIVER

-NFPHROPATHY, CHREBLE PROGRESSIVE,-

YPO_OHTPROTOTH

-FOCI OF MONOWICHERRORED S.-MINIMAL

LIVER (LT) : -FOCT OF MOS LUNG (LU) :

MINIMAL

NOTE: VEXTERNAL DRSERVATIONS: NONE

GENERAL INFORMATION (XX) :

NECROPSY

CLINICAL OBSERUATIONS

-APPEARED NORMAL

INFILTERITIE, LYMPHRID, SLIGHT

-PERIBRINCHIAL/PFRIVASIUI AR

THE FOLLOWING ORGANS WERE tINREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AN), ADRIA, THORACIC (AD), BINNE, FEMUR (FE), BIDNE, STERNIM (SB),

BRAIN WASTEM (BR), CECUM (CC), CORO, CORO, CORO, THYBAR (LC), CORO), THYBAR (LC),

BRAIN WASTEM (BR), ESPHAGUS (ES), EYE (BY), HEART (HT), ILEUM (IL), JEJUNDH (CS), KIDNEY (KD), LACRIMAL GL, EXO (FD),

LIVER (LT), LN, MESCHIERIC (MS), LN, OTHER (LN), THINS (LT), MANIMARY (CO), PANIMARS (PA), PARATHYRITO (PT),

MARROW, STERNUM (SE), MUSCLE, SKELETAL (SN), NERVE, SCIATIC (SN), OUARY (OU), PANIMARS (PA), PARATHYRITO (PT),

PITULIARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPI FIN (SP), STEMMACH, SI (ST), STIMMACH, MONES (SD),

THYMUS (TH), THYROIO (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT), ACOLLECTEDATARÉN (XM)

^{***} ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WFRE SAVED ***

APPENDIX 8 *** PATH/TOX SYSTEM OUTPUT *** SUBCHRONIC TOXICITY STINY IN RATS

PRINTED: 12-MAY-88 PASE: 347

STUDY NUMBER: 2399108

INDIVIDIJAL ANIMAL SUMMARY REPORT

RECORDER: SID JONES, DUM, PHD, DATUP MEJGHER: NOT REGALIRED BY PRITOROIL 29B.1 GRAMS SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE TERMINAL BODY METCHT: PATHOLOGIST: SID JONES, DUM, PED, DACUP STRIDY WEFFK OF DEATH: 14 PROSECTOR: DOUGLAS HERNDON DOSE GROUP: 3 STUDY DAY OF DEATH: 97 07/16/86 9:38 PROSE POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL SEX: FEMALE DATE AND TIME OF NECROPSY: DATE OF DEATH: 07/16/86 ANIMAL NUMBER: B08472

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

CLINICAL DBSERUATIONS

-APPEARED NORMAL

PATHOLOGY OBSFRUATIONS NECROPSY

^COLLECTED/TAKEN (XW):
-ELECTRON MICROSCOPY SAMPN F; LIUFR
GENERAL INFORMATION (XX):
>NOTE:>EXTERNAL OBSERUATIONS:NONE

-FORT OF MONTHAND FAR CELLS, - MINUMA

LIVER (LI) : -FINI OF MI) LUNG (LU) :

HISTOPATHOLOGY

INFILIRATION, LYMPHOLD, -54, 1GHT

-PERTBRONCHIAL/PERTUASCHLAR

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AN), BRNE, FEMUR (FE), BONE, STERNIM (SB), BRAIN WYSTEM (BR), CECUM (CE), COLON (CO), CORD, CFRVICAL (CS), CORO, FIMMAR (LC), CORD, THORACIC (TC), DUDDENUM (DU), ESOPHAGUS (ES), EYE (EY), HEARI (HI), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXO (ED), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LIMG (LU), MAMMARY GLAND (MS), MAND SALIVARY GL (SS), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), DVARY (DV), PANGREAS (PA), PARATHYRDID (PI), PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPLEFH (SP), STIMACH, SL (SI), STIMACH, NINGL (SU), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UR), UTERUS (UT) THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: KIONEY (KD)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOR) WARD SAVED ***

APPENDIX 8 *** PATH/IOX SYSTEM DUIPUL *** SUBCHRONIC TOXICITY STUDY IN RATS

PRINIFO: 12-MAY-88 PAGE: 348

INDIVIDUAL ANIMAL SUMMARY REPURT

STHDY NUMBER: 2399108

WEIGHER: NOT REQUIRED BY PRINTOLDIE 165.7 GRAMS RECLIRCOER: RARHARA DAY TERMINAL BODY WEIGHT: SACRIFICE STATUS: INISCHEDULED (D) PATHOLOGIST: NOT REDUITRED BY PROTOCOL STUDY WEEK OF DEATH: 2 PROSECTOR: BARBARA DAY DOSE GROUP: 3 STUDY DAY OF DEATH: 8 POST-FIX WEIGHER: NOT REDUIRED BY PROTOCOL DATE AND TIME OF NECROPSY: 04/18/86 15:45 DATE OF DEATH: 04/18/86 ANIMAL NUMBER: 808473

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

-ARTIFILLAR SURFACE NOT PRESENT, - PRESENT INFILTRATION, LYMPHOID. -SLIGHI -PERTERMENTALAL/PERTUASCIII AR -FORETGN MATERIAL, -PRESENT Y:IO_IOHTAGITEIH (FF) BONE, FEMILIA CENG CLD : DRSERUATIONS -MOTTLED; ALL LOBES, LIGHT TO DARK RED -FAILTIRE TO COLLAPSE; ALL LORES NOTE: > LAST IN-LIFE AND EXTERNAL GENERAL INFORMATION (XX) : DESERVATIONS: NONE NECROPSY PATHOLOGY CLINICAL OBSERVATIONS -APPEARED NORMAI

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDILLA (AM), ANRIA, THORACTE (AD), BOBE, FEMIRE (FE), ROBE, THORACTE (TD),
BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACTE (TD),
DUDDENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEIM (11), IEIMM (JE), KIDNEY (KN), LACRIMAE (S), EXE (EV),
LIVER (LT), LN, MESENTERIC (MS), LN, OTHER (LN), MAMMARY GLAND (MG), MAND SALIVARY (G. (SC), MARROW, STERNIM (SE),
MISCLE, SKELETAL (SM), NERUE, SCIATIC (SN), OVARY (TU), PARTERS (PA), PARTINGOLD (PI), PITHITARY (FI), RECHIM (TE),
SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), THYMUS (TH), THYRRO (TY),
TRACHEA (TR), URINARY BLANDER (UB), UTERUS (III), ACALLECTED/TAKEN (XM)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ATRIA, THORACIC (AU), BENE, STERNEM (SB), ERATH WASTEM (18), CFCUM (CC), CORD, CERUICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC), DUDDENUM (DE), ESOPHAMIS (ES), FYE (EY), HEART (HT), ILEUM (LL), JEJHNUM (GE), KIDNEY (KD), LACRIMAL GL, FXE (FD), LIVER (LT), LN, MESENIFRED (MS), MAND SALIVARY GL (SG), MARROW, STERNUM (SF), MUSCLE, SKELETAL (SM), NFRUE, STIATIC (SN), DUARY (DU), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PT), NFTHEM (SF), SKIM (SK), SCH (SP), STHMACH, GL (ST), STHMACH, MUSCLE (SU), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UR), UTERNS (HT)

*** ALL ORGANS/TISSUES (REDUIRED TO BE HARVESTED PER THE STIDY PROTOCOL) WFRE SAUED ***

SHRCHRONIC TOXICITY STUDY IN RAIS *** PATH/TOX SYSTEM DIJTPLIT *** APPENDIX B

PRINTED: 12-MAY-88 PAGE: 349

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NUMBER: 2399108

TERMINAL EDDY METGHT: 249.0 GRAMS RECORDER: SID JONES, DUM, PHD, DACUP SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE PATHOLOGIST: SID JONES, DUM, PHD, DACUP STUDY WEEK OF DEATH: 14 PROSECTOR: BARBARA DAY DOSE GROUP: 3 SEX: FEMALE DOS STUDY DAY OF DEATH: 96 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL 9:46 DATE AND TIME OF NECROPSY: 07/15/86 DATE OF DEATH: 07/15/86 ANIMAL NUMBER: B08474,

WETCHFR: NOT REGISELD BY PROTOCOR

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

CLINICAL DBSERVATIONS

-APPEARED NORMAL

OBSERUATIONS NECROPSY PATHOLOGY

-ELECTRON MICROSCOPY SAMPLE; I 19FR GENERAL INFORMATION (XX) : ACOLLECTED/TAKEN (XW) :

>NOTE:>EXTERNAL DBSFRUATIONS:NONE

INFILTRATION, LYMPHO10,-SLIGHT

-PFRICKTHEMINION /PFRICASSTER OR

CUNG CLUD :

HISTOPATHOLDISY

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRTA, THORACIC (AD), BINNE, FEMINE (FE), BINNE, STERNIM (SB), ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), CRND, CRND, LIMBAR (LC), CIRD, THORACIC (TC), BRAIN MASTEM (BR), CECUM (CO), CRC (CO), CRND, LACRIMAR (BL), BUNDENUM (DD), ESOPHAGUS (ES), EYE (EY), HEART (HI), ILLING (LI), DEJUNUM (DD), MARID SALIVARY (BL), PANCREAS (PA), PARATHYRBID (PI), PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPLFEN (SP), STIMACH, GL (ST), STIMACH, NORS (SH), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT) THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC FXAMINATION: KIDNEY (KD), LIVER (LI) 雅

*** ALL DRGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAULD ***

APPENDIX 8 *** PATH/INX SYSTEM CLITP:IT *** SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 19-MAY-88 PAGE: 3511

STUDY MIMER'S 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

DERNAL, CORTEX (AC), ADRENAL, MEDULLA (AN), AURTA, THORACIC (AD), BÜNE, FEMIR (FE), BÜNE, STERNIM (SR),
BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORD, CFRUTCAL (CS), CIRD, HIMBAR (LC), CORD, THORACIC (TC),
DUDOENUM (DI), ESÓPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNIM (JE), KIDNEY (KD), LACRIMAL GI, EXI (ED),
LIUER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LING (LU), MAMMARY GI AND (MS), MANY GI (SR),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERUE, SCIATIC (SN), DUARY (DV), PANCREAS (PA), PARATHYRNID (PI),
PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPIFFN (SP), STUMMAL, SIGNACH, NICHEL (SM),
THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UI), ACOLLECTEDATAKEN (XM) THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

^{***} ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WE'RE SAVED ***

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/TOX SYSTEM DUTPUT *** APPENDIX B

PRINTED: 19-MAY-88 PARF: 361

INDIVIDUAL ANIMAL SUMMARY REPORT

STLIOY NUMBER: 2399103

SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE PATHOLOGIST: SID JONES, DUM, PHD, DAILUP STUDY WEEK OF DEATH: 14 PROSECTOR: DOUGLAS HERNDON DOSE GROUP: 3 DEATH: 96 STUDY DAY OF POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL DATE AND TIME OF NECROPSY: 07/15/86 11:06 SEX: FEMALE DATE OF DEATH: 07/15/86 ANIMAL NUMBER: B08476

TERMINAL BODY WEIGHT: 249.2 GRAMS RETMEMPRES, DUM, PHD, DACUP WEIGHER: NOT REGILIRED BY PRITTED

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

CLINICAL DBSERVATIONS

-APPEARED NORMAL

OBSERVATIONS NECROPSY PATHOLOGY

STOMACH, GL. (ST) :

CIT)

UTERUS

INFILTRATION, LYMPHOID, -SLIGHT -PFRISRIBICHIAL/PFRIVASCHIAR -CONGESTION, -SLIGHT (ST): CONG CLED : STUMPLH, E -DARK ARFA; FUNDIC MICHSA, DARK RED -LUMEN, FLUID; BOTH HORNS, CLEAR

HISTOPATHOLOGY

COLLECTED/TAKEN (XW): -ELECTRON MICROSCOPY SAMPLE; LIVER GENERAL INFORMATION (XX): *COLLECTED/TAKEN

-DII ATATION, -MODERATE

UTERUS OID :

>NOTE:>EXTERNAL OBSERVATIONS:NONE ı

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRIA, THORACIC (AD), BONE, FEMUR (FE), BONE, STERNUM (SR), BRAIN WASTEM (BR), CECUM (CE), COTRO, DERVICAL (CS), CORD, LIMBOR (LC), CORO, CECUM (CE), MARIO (CE), MARIO (CE), MARIO (CE), MARIO (CE), MUSCLE, SKELETAL (SM), NEPUE, SCIATIC (SN), QUARY (QU), PANCREAS (PA), PARATHYROID (PI), PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

THE FOLLOWING TISSUES WERE INVEMARKABLE AT MICROSCOPIC EXAMINATION: KIDNEY (KD), LIVER (LI) *** ALL ORIGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STADY PROTOCOL) WERE SAVED ***

SUBCHRONIC TOXICITY STUDY IN RAIS *** PATH/TOX SYSTEM DUTPUT *** APPENDIX B

PRINTED: 12-MAY-88 PANT: 352

STUDY NIMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

SACRIFICE STATUS: SCHEDNLED, TERMINAL SACRIFICE
DF DEATH: 14 TERMINAL BNDY WEIGHT: 275.9 GRAMS
RECHROFE: SID INNES, OUM, PHD, DACUP STUDY WEEK OF DEATH: 14 DOSE GROUP: 3 STUDY DAY OF DEATH! 96 DATE AND TIME OF NECROPSY: 07/15/86 11:57 SEX: FEMALE DATE OF DEATH: 07/15/86

PRISECTOR: TIM GROUE

WEIGHER: NOT REQUIRED BY PROTOCOL PATHOLOGIST: SID JONES, DUM, PHO, DAILUP

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL

ANIMAL NUMBER: B08477

CLINICAL DBSERVATIONS

-APPEARED NORMAL

DBSERUATIONS NECROPSY PATHOLOGY

-ELECTRON MICROSCOPY SAMPLE; LIUFR ANDIE: SEXTERNAL DRSFRUATITINS: NONE GENERAL INFORMATION (XX): *COLLECTED/TAKEN (XW)

THE HITRATION, LYMPHAND, SELIGHT -PERTBRONCHIAL /PERTUASCIALAR

-NEPHRIPATHY, CHRIMIC PRIGRESSIVE,-

MINIMAL

HISTOPATHU DGY

THE FOLLOWING ORGANS LIERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AURTA, THORACIC (AD), BONE, FEMUR (FE), BONE, STERMON (SB),
BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LIMBAR (LC), CORD, LACRIMAL GL, EXO (EO),
DUDDENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), DEJUNIUM (JE), KIONEY (KO), LACRIMAL GL, EXO (EO),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (IN), LING (LI), MARMARRY GL MAND SALVORY GL (SS),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERUE, SCIATIC (SN), DUARY (DV), PANCREAS (PA), PARATHYRNIO (PI),
PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NUMBL (SID),
THYMUS (TH), THYROID (TY), TRACHEA (TR), LRIMARY BLACDER (TR), 11FRIS (HT)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: LIVER (LI) *** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTUCOL) WERE SAUFD ***

*** PATHATION SYSTEM DITTPLIT *** SUBCHRONIC TOXICITY STUDY IN RATS APPENDIX 8

PRINTED: 12-MAY-88 PAGE: 353

STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

SACRIFICE STATUS: INISCHEDULED (D) ANIMAL NUMBER: B08428 SEX: FEMALE DOSE GROUP: 3 SACRIFICE STATIL DATE OF DEATH: 04/20/86 STUDY OAY OF DEATH: 10 STUDY WEEK OF DEATH: 2 DATE AND TIME OF NECROPSY: 04/20/86 11:35 PROSECTOR: KIM LINCOLN PROTOCOL PATHOLOGIST: NOT REQUIRED BY PROTOCOL

WEIGHER: NOT REQUIRED BY PROTOCOM 180.2 GRAMS TERMINAL BOOY WEIGHT: 18
RECORDER: KIM LINCOLN

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

	PATHOLOGY OBSERVATIONS	
CLINICAL OBSERVATIONS	NECROPSY	HISTOPATHOLOGY
-APPEARED NORMAL	LUNG (LU): -FAILURE TO COLLAPSE; ALL LOMES, FLUID -FILED	EYE (EY) : >TISSHE MISSING >NOTE:>SEVERE ARTIFACT PRECLUDE
	-MOTTLED; ALL LOPES, LIGHT TO DARK RED GENERAL INFORMATION (XX):	TATERPRETATION KIDNEY (KD) :
	NOTE:>LAST IN-LIFE AND EXTERNAL COSEDIATIONS: MAST AT	-NEPHROPATHY, CHRONIC PROGRESSIVE;
	10:00 AM, FOLIND DEAD AT 11:30 AM	-PELUIS, DILATATION, -MIDERATE
		-PERIORPHIAL /PERIOASSIN AR,
		INFILTRATION, LYMPHOID, SI IGHT FOREIGH MATERIAL, PRESENT

VIISSUE MISSING RECTIM (RE) :

SUBCHRONIC TOXICITY STUDY IN RATS *** THITTEN SYSTEM BUILDIN *** APPENDIX 8

PRINTFO: 19-MAY-88

INDIVIDUAL ANIMAL SHMMARY REPORT

STUDY NUMBER: 2399108

SACRIFICE STATUS: UNSCHEDULED (D)	TERMINAL BROY WEIGHT: 180.2 GRAMS	RECORDER: KIM LINCON	LETGHER: NOT REQUIRED BY PROTOE	
DOSE GROUP: 3 SACRIFICE STATU	OF DEATH: 10 STUDY WEEK OF DEATH: 2	PROSECTOR: KIM LIMCALM	PATHOLOGIST: NOT REDUIRED BY PROTOCOL	
SEX: FEMALE	STIJDY DAY OF	04/20/86 11:35	IRED BY PROTOCOL	
ANIMAL NUMBER: B08478	DATE OF DEATH: 04/20/86	DATE AND TIME OF NECROPSY: 04/20/86 11:35	POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL	

DORENAL, CORTEX (AC), ADRENAL, MEDIILA (AM), AURIA, THURACIC (AD), BURIE, FEMIR (FF), BORIE, STERNUM (SB),
BRAIN (M.STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THURACIC (TC),
BUDDENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEIM (IL), ISTIMUM (JE), KIDNEY (KD), LAFRIMAN EI, FXG (FG),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE),
MUSCLE, SKELETAL (SM), NERUE, SCIATIC (SN), DVARY (CV), PANCREAS (FA), PARAIHYRDID (PT), PITHITARY (PI), FECTHM (RF),
SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, GL (ST), THYMUS (TH), THYRDID (TY),
TRACHEA (TR), URINARY BLADDER (UB), UTERUS (HT), ACOLLECTED/TAKEN (XW) THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDILLA (AT), AGIRTA, THORACIC (AD), BINNE, FEMIRE (EE), FONE, STERNIM (SB), BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC), DUODENUM (OU), ESOPHAGUS (ES), HEART (HT), ILEIM (IL), DEJINNIM (DE), LAFRIMAL EL, FXD (FO), LIVER (LT), LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNIM (SE), MISCLE, SKFLETAL (SM), NERUE, SCIATIC (SN), OUARY (OU), PANCREAS (PA), PARATHYROID (PT), PITHIDARY (PT), SKIN (SK), SPLETA (SP), STOMACH, GL (ST), STOMACH, GL (ST), UTERHS (HT) FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: 표

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTUKOL) WERE SAUED ***

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/IOX SYSTEM (MITPHIT *** APPENDIX B

PRINTED: 12-MAY-88

INDIVIDUAL ANIMAL SHMMARY REPORT

STIDY MINDER: 2399108

WETGHER: MOT REQUIRED BY PROTOCON TERMINAL BODY WEIGHT: 24 RECORDER: DAY SACRIFICE STATUS: UNSCHEDULED (D) PATHOLOGIST: NOT REGUIRFO BY PROTOCOL STUDY WEEK OF DEATH: 14 PROSECTOR: RARBARA DAY DOSE GROUP: 3 DEATH: 96 STUDY DAY OF POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL DATE AND TIME OF NECROPSY: 07/15/86 11:59 SEX: FEMALE DATE OF DEATH: 07/15/86 ANIMAL NUMBER: B08479

HISTOPATHOLOGY

INFILTRATION, LYMPHOID, -SLIGHT -PFRTERRINGHINTAL / PERTUASITUR AR -FORETHAN MATERIAL, - PRESENT

LUNG CLED :

CLINICAL DBSERVATIONS

-APPEARED NORMAL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

PATHOLOGY OBSERUATIONS NECROPSY

-MOTTLED; ALI LOBES, LIGHT TO DARK RED -FAILURE TO COLLAPSE; ALL LORES ANDTE: ALAST IN-LIFE AND EXTERNAL GENERAL INFORMATION (XX) : **:** ∃∃

CIESERUAT ICINS: NONE

THE FOLLOWING DRGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRIA, THORACIC (AC), BINE, FEMUR (FE), BONE, STERNUM (SB),
ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRIA, THORACIC (CS), FURD, LIMMARY (LD), CIRD, THORACIC (TE),
DUDDENIM (OU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEDINIM (JE), KIDNEY (KD), LACRIMAL GL, EXO (FO),
DUDDENIM (OU), ESOPHAGUS (ES), EYE (EY), MAMMARY GLAMO (MG), MAMMARY GLAMO (SC), MARGINE, STERNUM (SE),
MUSCLE, SKELETAL (SM), NERUE, SCIATIC (SN), DUARY (OU), PANCREAS (PA), PARATHYRHO (PT), PITHITARY (PI), RECTHM (RF),
SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NORS (SD), 144MHS (TH), 144KOLD (TY),
TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT), ^COLLECTED/TAKEN (XW)

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AD), BONE, FEMUR (FE), BONE, STERNUM (SR),
BRAIN WASTEM (BR), GECUM (CE), COLON (CD), CORD, CERVITAL (FS), CORD, LINEAR (FC), CARO, LACRIMAL GL, EXO (ED),
DUDDENUM (DD), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXO (ED),
LIVER (L), LN, MESENTERIC (MS), MAMMARY GLAND (MS), MAND SALIVARY GL (SS), MARRIEL, STYREUM (SF), MISCUE, SKELETAL (SM),
NERUE, SCIATIC (SN), DUARY (DU), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), RECTUM (RE), SKIM (SK),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), THYMUS (TH), THYROID (TY), TRACHEA (TR), URIHARY BIADDER (18), THE FOLLOWING TISSUES WERE INREMARKABLE AT MICROSCOPIC EXAMINATION: UTERUS (UT)

*** ALL DRGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STIDY PROTOCOL) WERE SAULD ***

SUBCHRONIC TOXICITY STUDY IN RATS *** PATHZIOX SYSIEM DITIPLIT *** APPENDIX 8

PRINTED: 39-MAY-88 PAGE: 354

INDIVIDUAL ANIMAL SUMMARY REPTRT

STREET STREET STREET

TERMINAL BROY WEIGHT: 257.7 GRAMS RECREBER: SID JONES, DUM, PHD, DACUP 257.7 GRAMS SACRIFICE SACRIFICE STATUS: SCHEDNLFD, TERMINAL PATHOLOGIST: SID JONES, DUM, PHD, DACUP STUDY WEEK OF DEATH: 14 PROSECTOR: DOMEIAS HERMOON DOSE GRAND: 3 STUDY DAY OF DEATH: 97 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL SEX: FEMALE DATE AND TIME OF NECROPSY: 07/16/86 11:03 DATE OF DEATH: 07/16/86 ANIMAL NUMBER: B08480

WEIGHER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

HISTOPATHOLOGY OBSERUATIONS -ELECTRON MICROSCOPY SAMPLE; I IVER NECROPSY *COLLECTED/TAKEN (XW) PATHOLOGY CLINICAL D'ESERVATIONS -APPEARED NORMAL

ANDTE: SEXTERNAL DRSFRUATIONS: NOW GENERAL INFORMATION (XX):

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRTA, THORACIC (AD), BONE, FEMUR (FE), BONE, STERNIM (SB),
BRAIN WASTEM (BR), CECUM (CE), COLON (CD), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUDDENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), DEJUNUM (JE), KIONEY (KD), LACRIMAL GL, EXD (ED),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LING (LU), MAMMARY HIGHD (MS), MAND SALIVARY HIGHER (SR),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERUE, SCIATIC (SN), QUARY (DU), PANCREAS (PA), PARATHYROID (PT),
PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPIFFN (SP), STOMACH, GL (ST), STOMACH, HIMMAL (SD),
THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT) THE FOLLOWING ORGANS MERE LINREMARKABLE AT MECROPSY:

FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: HEART (HT), KIDNEY (KD), LIVER (LI), LUNG (LU) 뿔

*** ALL ORGANS/IISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCUL) WERE SAVED ***

SUBCHRONIC TOXICITY STIJOY IN RATS *** PATH/TOX SYSTEM DUIPUT *** APPENDIX 8

PRINTED: 12-MAY-88

INDIVIDUAL ANIMAL SHIMMARY REPORT

STUDY MIMBER: 93994118

SACRIFICE STATUS: SCHEDUIED, TERMINAL SACRIFICE TERMINAL BODY METCHT: PATHOLOGIST: SID JONES, DUM, PHD, DACUP STUDY WEEK OF DEATH: 14 PROSECTOR: HARBARA DAY DOSE GROUP: 3 DEATH: 97 STUDY DAY OF POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL DATE AND TIME OF NECROPSY: 07/16/86 11:41 DATE OF DEATH: 07/16/86 ANIMAL NUMBER: BUB481

RECORDER: SID JONES, DUM, PHD, DACUP WETGHER: NIT REDUIRED BY PRITTING 259.0 GRAMS

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

CLINICAL DBSERVATIONS

-APPEARED NORMAL

O B S E R U A T L O N S NECROPSY PATHOLOGY

INFILTRATION, LYMPHOID, -SLIGHT LUNG (LU): -- PERTUASIUM AR

HISTOPATHOLOGY

MANUEL MEXTERNAL DRISERVATIONS MONE GENERAL INFORMATION (XX) :

-ELECTRON MICROSCOPY SAMPLE; 11UFR

~COLLECTED/TAKEN (XW)

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRIA, THORACIC (AD), BINE, FEMUR (FE), BONE, STERNIM (SR),
BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LIMBAR (LC), CORD, THORACIC (TC),
DUDDONUM (DU), ESOPHABUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GI, EXO (FO),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LING (LD), MAMMARY GI AND (MS), MAND SALIVARY GI, (SS),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERUE, SCIATIC (SN), OVARY (DV), PANCREAS (PA), PARATHYRIJO (PI),
PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SP FFN (SP), STIMACH, GI (ST), STIMACH, NORGH, GI (SI),
THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT)

FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: KIDNEY (KD), LIVER (LI) 뿔

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) MERE SAUFD ***

APPENDIX 8 *** PATH/TOX SYSTEM CHITPHT *** SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 10-MAY-80 PAGE: 358

STHDY NUMBER: 2399100

INDIVIDIAL ANIMAL SIMMARY REPORT

ANIMAL NUMBER: B08502 SEX: FEMALE DATE OF DEATH: 07/14/86 STUDY DAY OF DATE AND TIME OF NECROPSY: 07/14/86 11:11 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL	ОЕАТН	DOSE GROWE: 4 SACRIFICE STATUS: : 95 STUDY WEEK OF DEATH: 14 PROSECTOR: TIM GROVE PATHOLOGIST: SID JOHES, DUM, PHD, DACUP	SCHE	OUR FD, TERMINAU SACRIFISE INAL BODY WEIGHT: 259.9 GRAMS RECURDER: SID JONES, DOM, PHO, DACUP WEIGHFR: IIM GROUE
ORGÁN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	DRGAN WETGHT RELATIVE TO BODY WETCHT (%)	ORGAN TO BRAIN MFJGHT RATIO	ORGAN
ADRENAL (AD) DUARY (DU) BRAIN MASTER (RR)	. 066 . 096 1.84	. 0254 % . 0370 % . 217 %	. 0516	LEIGHT TOKEN LIFIGHT TOKEN LIFIGHT TOKEN
	. 77 . 53 1.93 7.14	.296 % .283 % .742 % 2,747 %	. 283 1.035 3.830	
CLINICAL OBSERUATIONS	G	Y 0 8 S E	i	HISTOPATION ONLY
-APPEARED NORMAL	GENERAL JAN	NERAL INFORMATION (XX): >NOTE:>EXTERNAL OBSERVATIONS:NONE	ROWE, FEMINE (FF); -ARTICULAR SURFACE KIDNEY (ND); -NEPHRIDATHY, CHRON MINIMAL LINES (LID); -PERIBRONCHIAL/PERI THETTEATTON, 1 YMP UTERUS (UT);	NE, FEMURE (FF); -ARTICULAR SURFACE NOT PRESENT,-PRESENT -NEPHRIPATHY, CHROWIC PROGRESSIVE,- MINIMAL HS (11); -PERIBRONCHIAL/PERIVASCULAR; THETTEATTOR, 1 YMPHOTO,-SLIGHT -OTLATATOR, 13 MPHOTO,-SLIGHT

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/TOX SYSTEM DIDDID *** APPENDIX 8

PRINIFD: 12-MAY-88 PAITE: 359

INDIVIDINAL SUMMARY REPURT

STUDY MUMBER: 2399108

TERMINAL BODY WFIGHT: 259.9 GRAMS RECORDER: SID ADMES, DUM, PHD, DACUP SACRIFICE STATUS: SCHEDINED, TERMINAL SACRIFICE WEIGHER: TIM GROUE PATHOLOGIST: SID JONES, DUM, PHO, DACUP STIIDY WEEK OF DEATH: 14 PROSECTOR: TIM GROVE DOSE GROUP: 4 STUDY DAY OF DEATH: 95 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL SEX: FEMALE AND TIME OF NECROPSY: 07/14/86 11:11 DATE OF DEATH: 07/14/86 ANIMAL NUMBER: B08502 DATE

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ATRIA, THORAGIC (AN), ROBE, FEMIR (FE), ROBE, STERNIM (SB),
BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORO, CERVICAL (CS), CORO, LUMBAR (LC), CORO, THORAGIC (TC),
DUDDENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ITEUM (TL), DELINHEM (DE), KIDMEY (KO), LACRIMAL GI, FAO (FO),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GI (SG),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERUE, SCIATIC (SN), OVARY (DO), PANGREAS (PA), PARATHYRRID (PT),
PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, GL (ST),
THYMUS (TH), THYRDID (TY), TRACHEA (TR), HRINARY BLADDER (1M), HTERUS (HT), ACCULECTED/TAKEN (XM)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDILLA (AM), AORTA, THORACIC (AD), BONE, SIFRNIM (SB), BRAIN W.STFM (BR), LFCHM (CF), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC), DUDDENUM (DU), ESOPHABUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJINUM (JE), LACRIMAL BL, FXO (ED), LIVER (LT), LA, MESFNIFRIC (MS), MAMMARY BLAND (MS), MAMMAROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), DVARY (DV), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), RECTUM (RE), SKIN (SK), SPI EFN (SP), STOMACH, RINKAL (SD), HUKAL (SD), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB)

*** ALL. ORGANS/IISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

APPENDIX 8 *** PATH/TOX SYSTEM GUTFUL *** SUBCHRONIC TOXICITY STUDY IN RATS

INDIVIDIDAL ANIMAL SHMMARY REPORT

12-MAY-86	
TOMERING	PAISE:

STUDY HUMBER: 2399108

ANIMAL NUMBER: 808503 SEX: FEMALE DATE OF DEATH: 07/14/86 STUDY DAY OF DEATH: DATE AND TIME OF NECROPSY: 07/14/86 13:19 POST-FIX WEIGHER: NOT REGULIRED BY PROTOCOL P	SEX: FEMALE DOSE GR STUDY DAY OF DEATH: 95 14/86 13:19 PROSECTOR BY PROTOCOL PATHOLOGI	DOSE GROUP: 4 . SACRIFICE STATUS: 95 STUDY WEEK OF DEATH: 14 PROSECTOR: BARBARA DAY	SCHE	DULED, TERMINAL SACRIFICE INAL BODY WEIGHT: 235.2 GRAMS RECORDER: SID JUNES, DUM, PHD, DACUP WEIGHER: BARBARA DAY
ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO RODY WEIGHT (%)	ORSAN TO BRAIN METSHT RATIO	0 R G A N S T A T U S
ADRENAL (AD)	.061	, 0259 %	6020	
DUARY (DU)	.099	. 0420 %	. 85113 1.000	LETICHT TAKEN
	.72	% 90¢.	692.	
SPLEEN (SP)	.50	.214 %	.256	
KIDNEY (KD)	1.74	% 6£4°	.885	LETCHT TAKEN
LIVER (LI)	6.89	2.931 %	3.510	WEIGHT TAKEN
CLINICAL OBSERUATIONS	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	OGY OBSERUALI	S Z C	HISTOPATION OGY
-АРРЕЯКЕО КОКМАЦ	GENERAL INFO	GENERAL INFORMATION (XX): >NOTE:>EXTERNAL DRSERVATIONS:NONE	FYE (EY): -CHRONIC INFLAMMATI SLIGHT CLIN: (LID): -PERIBRONCHIALZPERI INFLITRATION, LYMP UTERUS (UT): -OTLATAGET	E (EY): -CHRONIC INFLAMMATION, HARDERIAN GLAND, SLIGHT NG (LID): -PERIBRONCHIAL/PERIVASCULAR; INFLIRATION, LYMPHOLD,-SLIGHT -CRUS (UT): -OHI ALATION, LYMPHOLD,-SLIGHT

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/TOX SYSTEM OUTPIT *** APPENDIX 8

PRINTFD: 19-MAY-88 PAGE: 361

STUDY RUMBER: 9399108

INDIVIDUAL ANIMAL SUMMARY REPORT

RECORDER: SID JONES, DUM, PHD, DACUP 235.2 GRAMS SACRIFICE STATUS: SCHFOWLFD, TERMINAL SACRIFICE WEIGHER: BARBARA DAY TERMINAL BODY METGHT: PATHOLOGIST: SID JONES, DUM, PHD, DAIJUP STUDY WEEK OF DEATH: 14 PROSECTOR: HARBARA DAY DUSE GROUP: 4 STUDY DAY OF DEATH: 95 POST-FIX WEIGHER: NOT REGIJIRED BY PROTOCOL DATE AND TIME OF NECROPSY: 07/14/86 13:19 DATE OF DEATH: 07/14/86 ANIMAL NUMBER: B08503

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDILLA (AM), ADRIA, THORACIC (AD), BONE, FEMIR (FE), BONE, STERNIM (FB),

BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORO, CERVICAL (CS), CORO, LUMBAR (LC), CORO, THORACIC (TC),

BRAIN WASTEM (BR), CECUM (CE), CY, HEART (HT), ILEUM (II), JENNIM (JE), KIDNEY (KD), LACRIMAL GI, FXO (FO),

LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG), MAND SALIUARY GI, MAND SALIUARY GE), MUSCLE, SKELETAL (SM), NERUE, SCIATIC (SM), PARCREAS (FA), PARCREAS (FA), PARCREAS (FA), PARCREAS (FA), PARCREAS (FA), NOMSI (SD),

PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, GL (ST),

THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UR), UTERIS (UT), ACOUTECTED/TAKEN (XM)

ADRENAL, CORTEX (AC), ADRENAL, MEDILLA (AM), AORTA, TYDRACIC (AD), ACHE, FFMIR (FE), BRHE, STERNIM (SA),
BRAIN W/STEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), ESDPHAGUS (ES), HEART (HT), ILFIM (11), JEJUNIM (JE), KIDNEY (KD), FACRIMA (R., FXD (FO),
LN, MESENTERIC (MS), MAMMARY GLAND (MS), MAND SALIVARY GL (SG), MARROW, STERNUM (SF), MISCLE, SKELETAL (SM),
NERUE, SCIATIC (SN), OUARY (DU), PANCREAS (PA), PARATHYROLD (PI), PITHITARY (PI), RECTUM (KE), SKIN (SK),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), THYMUS (TH), THYROLD (TY), TRACHEA (TR), URINARY BIADDER (JR) FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: 포

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/TOX SYSTEM OUIPUT *** APPENDIX B

PRINTFOR 12-MAY-88 PAISE: 362

INDJUTQUAL ANIMAL SUMMARY REPORT

STUDY MIMRER: 2399108

TERMINAL BODY WEIGHT: 728.2 GRAMS RECORDER: SID JONES, DUM, PHD, DACUP SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE PATHOLOGIST: SID JONES, DUM, PHD, DACUP STUDY WEEK OF DEATHS 14 PROSECTOR: DOUGLAS HERNDON DOSE GROUP: 4 STUDY DAY OF DEATH! 95 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL DATE AND TIME OF NECROPSY: 07/14/86 10:20 SEX: FEMALE DATE OF DEATH: 07/14/86 ANIMAL NUMBER: 808504

WEIGHTR: WIT REWIIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

HISTOPATHOLOGY CUNG (11) : **DBSERUATIONS** -ELECTRON MICROSCOPY SAMPLE; LIUFR NOTE: SEXTERNAL OBSERVATIONS: NOME GENERAL INFORMATION (XX): NECROPSY COLLECTED/TAKEN (XW) : PATHOLOGY CLINICAL OBSERVATIONS

INFILTRATION, LYMPHOID, -SI IGHT -PERTHRUMENTAL ZPERTUASIUM AR

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRIA, THORACIC (AD), BONE, FEMUR (FE), BONE, STERRIM (SB),
BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LHMBAR (LC), CORD, THORACIC (TC),
BUDDENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNIM (JE), KIONEY (KD), LACRIMAL GI, EXO (ED),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LING (LU), MAMMARY GLAND (MS), MAND SALIVANY GI, ES),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERUE, SCIATIC (SN), DVARY (DV), PANCREAS (PA), PARATHYROID (PT),
PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN (SK), SKIN (SK), SKIN (SK), SKIN (SK), UTIMARY BLADDER (UB), UTERUS (UT) THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

DUBDENUM (DU), ESÓPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIÖNEY (KD), LAGRIMAL GL, EXD (FD), LIVER (LI), LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SR), MARKHUM (SF), RIBGLE, SKLETAM (SM), NERVE, SCIATIC (SN), DVARY (DU), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), RECTUM (RF), SKIN (SK), SKIN (SK), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NINGL (SH), THYMIS (TH), THYROID (TY), TRACHEA (TR), TRINARY SHADSER (TR), ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AD), BONE, FEMUR (FE), BONE, STERNUM (SB), BRAIN WYSTEM (BR), CECUM (SE), COLON (CO), CARD, CFRVICAL (CS), LORD, LUMBAR (LC), LURD, THURACIC (TC), FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: UTERUS (UT) 里

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAUED ***

A** PATH/TOX SYSTEM DUTPUT *** SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-RE PAGE: 363

INDIVIDUAL ANIMAL SHMMARY REPORT

STIEDY NUMBER: 2399108

WEIGHER: NOT REDUIRED BY PRITIDIN TERMINAL BODY WEIGHT: 17 SACRIFICE STATUS: UNSCHEDULED (D) PATHOLOGIST: NOT REQUIRED BY PROTOCOL H: 11 STUDY WEEK OF DEATH: 2 PROSECTOR: BARBARA DAY DOSE GROUP: 4 ANIMAL NUMBER: 808505 SEX: FEMALE DOST DATE OF DEATH: 04/21/86 STUDY DAY OF DEATH: 11 DATE AND TIME OF NECROPSY: 04/21/86 15:05 PROSEI POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL

*** ANIMAL HAS NO DRGAN WEIGHTS RECORDED ***

CLINICAL OBSERVATIONS	PATHOLOGY OBSERVATIONS NECROPSY	HISTOPATHOLOGY
-APPEARED NORMAL	LACRIMAL GL, EXO (ED): -DARK AREA; LEFT, MULTIPLE, DARK RED, PINPOINT LUNG (LU): -FAILURE TO COLLAPSE; ALL LOBES -MOTTLED; ALL LOBES -MOTTLED; ALL LORES, LIGHT TO DARK RED GENERAL INFORMATION (XX): >NOTE:>LAST IN-LIFE AND EXTERNAL GASPING, DIFD AFTER (MISTAGE GAUAGE	ADREMAL, MEDILLA (AM): -IRII ATERALY EXAMINED,-PRESENT BONE, FEMUR (FE): -ARTICAL ACT SHEFACE HIT PRESENT,-PRESENT LACRIMAL GL, EXD (ED): >UNREMARKABLE LING (LI): -PERIBRONCHIAL PERIOASCIN AR; INFILTRATION, LYMPHOLO,-SI IGHT -FONE IGH MATERIA;-PRESENT PARATHYROLO (PT): >SECTION EXAMINED; TISSHE NOT PRESENT

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/10X SYSTEM DUTPUT *** APPENDIX 8

PRINTED: 12-MAY-80 PAISE: 364

STRIDY NUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

175.2 GRAMS RECORDER: PARBARA DAY TERMINAL BODY MFIGHT: SACRIFICE STATUS: UNSCHEDULED (D)

WEIGHER: NOT REQUIRED BY PROTOCOL PATHOLOGIST: NOT REGUIRED BY PROTOCOL PROSECTOR: BARBARA DAY DATE OF DEATH: 04/21/86 STUDY DAY OF DATE AND TIME OF NECROPSY: 04/21/86 15:05 POST-FIX WEIGHER: NOT REGUIRED BY PROTOCOL

STUDY WEEK OF DEATH: 2

DOSE GROUP: 4

DEATH: 11

SEX: FEMALE

ANIMAL NUMBER: B08505

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDJILA (AM), ANRTA, THORACIC (AM), ROBE, FEMUR (FF), ROBE, STERNUM (SB),

BRAIN WISTEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),

BRAIN WISTEM (BN), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (LL), JEGINAM (JE), KIDNEY (KD), LIVER (LT),

LN, MESENTERIC (MS), LN, OTHER (LN), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROM, STERNUM (SE),

MUSCLE, SKELETAL (SM), NERUE, SCIATIC (SN), DUARY (DV), PANERFAS (PA), PARATHYROID (PT), PITHITARY (PT),

SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SD), THYMUS (TH), THYROID (TY),

TRACHEA (TR), URINARY BLADDER (HB), UTERUS (HT), ^COLLECTED/TAKEN (XM)

ADRENAL, CORTEX (AC), AORTA, THORACIC (AD), BONE, STERNIM (SB), BRAIN LAYSTEM (BR), CECHM (CE), COLON, HEART (HI), CORD, CERVICAL (CS), CORO, LUMBAR (LC), CORD, THORACIC (TC), DIDDENIM (DI), ESOPHAGUS (ES), EYE (EY), HEART (HI), ILEUM (IL), JEJUNUM (JE), KIONEY (KD), LIVER (II), IN, IN, MESENTERIC (MS), MAMMARY GLAND (MS), MAND SALIVARY (R (SB), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), DUARY (DV), PANCREAS (PA), PITHITARY (PI), RECTUM (RE), SKIN (SK), SPLEEN (SP), STOMACH, BL (ST), STOMACH, NONAX. (SH), THYMIS (IH), THYROLD (TY), TRACHER (TR), THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: URINARY BLADDER (UB), UTERUS (UT)

*** ALL DRGANS/TISSUES (REDUIRED TO BE HARVESTED PER THE STIDY PROTOCOL) WERE SAVED ***

APPENDIX 8 *** PATH/IDX SYSTEM GITPUT *** SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-RS PAGE: 365

STIEDY MIMBER: 2399108

INDIVIDIAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: B08506 SEX: FEMALE DATE OF DEATH: 07/14/86 STUDY DAY OF DATE AND TIME OF NECROPSY: 07/14/86 14:16 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL	- DEATH	DOSE GROWP: 4 SACRIFICE STATUS: 95 STUDY WEEK OF DEATH: 14 PROSECTOR: BARBARA DAY PATHOLOGIST: SID JONES, DUM, PHD, DACUP	#03 11 11 11	DULED, TERMINAL SACRIFICE INAL BODY WEIGHT: 230.9 GRAMS RECORDER: SID JUNES, DVM, PHO, DACUP WEIGHER: BARBARA DAY
ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN WEIGHT RATIO	ORGANSTORE
ADRENAL (AD) DUARY (DU) BRAIN W/STEM (BR) HEART (HT) SPLEEN (SP) KIONEY (KD) LIUER (LI)		.0252 % .0479 % .851 % .320 % .233 % .788 % 3.595 %		METCHT TAKEN WETCHT TAKEN WETCHT TAKEN WETCHT TAKEN WETCHT TAKEN WETCHT TAKEN
CLINICAL OBSERVATIONS	₽	HOLOGY ORSFRUATI NECROPSY	ากหร	HISTOPATHOLOGY
-APPEARED NORMAL	STOMACH, NONGL (SU): -WALL, THICKENED -MALL, THICKENED -RAISED AREA; TWD, GENERAL INFORMATION (STOMACH, NONGC (SU): -WALL, THICKENED -RAISED AREA; TWD, WHITE, 3 X 3 MM -RAISED AREA; TWD, WHITE, 3 X 3 MM GENERAL INFORMATION (XX): >NOTE:>EXTERNAL OBSERVATIONS:NONE	E	: -D,-PMESFNT ' N, HARDFRIAN GLAM ASCILAR, DID,-SLIGHT F.

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/IOX SYSTEM DUTPUT *** APPENDIX 8

INDIVIDUAL ANIMAL SUMMARY REPORT

PRINTEDS 19-MAY-88 PACE: 366

STHINY MIMPER: 9399111R

SACRIFICE STAIMS: SCHEDULED, TERMINAL SACRIFICE TERMINAL BODY WFIGHT: PATHOLOGIST: SID JONES, DUM, PHO, DACUP STUDY WEEK OF DEATH: 14 PROSECTOR: RARBARA DAY DOSE GROUP: 4 SEX: FEMALE DOS STUDY DAY OF DEATH: 95 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL DATE AND TIME OF NECROPSY: 07/14/86 14:16 DATE OF DEATH: 07/14/86 ANIMAL NUMBER: B08506

RECORDER: SID JONES, DUM, PHD, DACUP WEIGHER: BARBARA DAY

230.9 GRAMS

LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MANMARY GLAND (MS), MAND SALIVARY G. (SS), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SM), NUARY (DV), PAKERES (PA), PAKERES (TA), THYROLD (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (LT), ACHLECTED/TAKEN (SM) ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ANRTA, THORACIC (AD), RINNE, FFMIR (FE), BONE, STERNIM (SB), BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LIMBAR (LC), CORD, THORACIC (TC), DUODENUM (OD), ESOPHAGUS (ES), EYE (EY), HEART (HT), NEIM (H), NEIM MIM (AF), KIONEY (KD), SACRIMAL BL), EXO (FD), THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: 표

ADRENAL, CORTEX (AC), AGRIA, THORACIC (AD), BONE, FEMIR (FF), BONE, STERNIM (SB), BRAIN WYSTIM (SB), CETSIM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC), DIDDENUM (DE), ESOPHASIS (ES), MEART (HI), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL (BL, EXO (EO), 110FR (LI), 111, MESPUTFRIC (MS), MARROW, STERNUM (SE), MISCLE, SKELETAL (SM), NERUE, SCHATIC (SN), DUARY (OV), PARICREAS (PA), PARATHYROID (PT), PITUITARY (PI), RECTUM (RE), SKIN (SK), SPLFIN (SP), STOMACH, SL (SI), LIYMIS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/TIN SYSIFM DIMFNI *** APPENDIX B

PRINTED: 12-MAY-RO PAINE: 34.7

INDIVIDUAL ANIMAL SUMMARY REPURT

STIEDY NUMBER: 2399108

TERMINAL BODY WEIGHT: 258.4 GRAMS
RECORDER: SID JONES, DUM, PHD, DACOP
WEIGHER: NOT REDUIRED BY PROTITING SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE PATHOLOGIST: SID JONES, DVM, PHD, DACVP STUDY WEEK OF DEATH: 14 PROSECTOR: DOLIGHAS HERHDON DOSE GROUP: 4 DEATH: 95 STUDY DAY OF POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL SEX: FEMALE DATE AND TIME OF NECROPSY: 07/14/86 11:41 DATE OF DEATH: 07/14/86 ANIMAL NUMBER: 808507

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

	PATHOLOGY ORSERVATIONS	
CLINICAL OBSERVATIONS	NECROPSY	HISTOPATHOLDS
-APPEARED NORMAL	^COLLECTED/TAKEN (XW): -ELECTRIN MICRISCOPY SAMPLE; LIVER GENERAL INFORMATION (XX): >NOTE:>EXTERNAL DBSERVALIDUS:NONE	BONE, FEMURE (FE): -ARTICULAR SLUGACE NOT PRESENT,-PRESENTURE (LID: -PRESENTATION, LYMPHOIDSLIGHT
THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:	AT NECROPSY:	

Ξ

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AD), BONE, FEMIR (FE), BONE, STERNIM (SB),
BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORD, CERUICAL (CS), CORD, THORACIC (TC),
DUDDENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), DEDUNUM (DE), KIDNEY (KD), LACRIMAL GL, EXO (ED),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUMG (LI), MAMMARY GLAND (MS), MAND SALIVARY GL (SB),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERUE, SCIATIC (SN), QUARY (DU), PANCREAS (PA), PARATHYROID (PI),
PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN (SK), DIHER (SS), SPLEFN (SP), STOMACH, GL (SI), STOMACH, NORMAL (SO),
THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT)

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ANRIA, THORACIC (AC), BONE, STERNIM (SR), BRAIN W/STEM (BR), CFCIM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CHON, THURSHIM (ND), ESPHARIS (FS), EYF (FY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIDNEY (KD), LACRIMAL GL, EXO (ED), LIVER (LI), LN, MESENTERIC (MS), MARRIL, STERNIM (SF), MISCIE, SKELFTAL (SM), MERUF, SCIATIC (SN), DANDARY GLAND (MG), PANCREAS (PA), PARATHYROID (PI), PITULIARY (PI), RECIUM (RF), SKIN (SK), SPLEEN (SP), STOMACH, G1 (ST), STOMACH, NONGL (SU), THYMUS (TH), THYROID (TY), TRACHEA (TR), HRIBARY BEADDER (HB), HIFREE (HD) FOLLOWING TISSUES MERE UNREMARKABLE AT MICROSCOPIC FXAMINATION: 里

*** ALL ORGANSZIJES (REQUIRED TO BE HARUFSTED PER THE STIMY PROTRIBL) WERE SAUFD ***

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/TOX SYSTEM fillfill *** APPENDIX 8

PRINTED: 19-MAY-88 PAGE: 368

INDIVIDIDAL ANIMAL SIMMARY REPORT

STHEP MINGER: 9399108

TERMINAL BIDY METGHT: 233.2 GRAMS RECREBER: SID JONES, DUR, PHD, DACUP WEIGHER: NOT REQUIRED BY PROTOCOL SAIRTFILE STATUS: SCHEDINED, FERMINAL SAURTETE PATHOLOGIST: SID JONES, DUM, PHD, DACUP STUDY WEEK OF DEATH: 14 PROSECTOR: DOUGLAS HERNOWN DUSE GROUP: 4 STUDY DAY OF DEATH: 95 DATE AND TIME OF NECROPSY: 07/14/86 14:26 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL AND TIME OF NECROPSY: 07/14/86 14:26 SEX: FEMALE DATE OF DEATH: 07/14/86 ANIMAL NUMBER: 808508

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

------CLINIGAL OBSERVATIONS

- APPEARED NORMAL

O B S E R U A T I D N S NECROPSY PATHOLOGY

-ELECTRON MICROSCOPY SAMPLE; LIVER SNOTE: SEXTERNAL DESFROAT LONS: NORIE GENERAL INFORMATION (XX) : ~COLLECTED/TAKEN (XW) :

1

INFILTRATION, LYMPHOID,-MINIMAL - PERTHAMBAL ZPERTUASILIL AR HERRS CHI: LUNG CLED :

HISTOPATHOLOGY

-DILATATION, -SLIGHT

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AD), BINE, FEMUR (FE), BONE, STERNIM (SR), BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LIMBAR (LE), KIONEY (KD), LATRIMAL BL, EXO (ED), DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIONEY (KD), LATRIMAL BL, EXO (ED), NAMEMARY GLOTS, MAIN SALIVARY BL (SR), NAMEMARY GLOTS, MAIN SALIVARY BL (SM), DOARY (DV), PANCREAS (PA), PARATHYROLD (PT), MARROW, STERNUM (SE), MISCLE, SKELETAL (SM), OR SCIPTIC (SN), DOARY (DV), PANCREAS (PA), PARATHYROLD (PT), PANCREAS (PA), RECTUM (RE), SKIN (SK), SKIN, OTHER (JE), STIMACH, MARGE (SE), THYMUS (TH), THYMUS (THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRIA, THORACIC (AD), BONE, FEMIR (FE), BONE, STERNIM (SB),
BRAIN WASTEM (BR), CECUM (CE), COLON (CD), CORD, CRUTCAL (CS), CORD, LIMBAR (LD), ENDREY (KD), LACRIMAL SI, EXO (ED),
DUDDENUM OUD, ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJONIM (AS), MARKOTA, STERNIM (SF), MINSLE, SKIFFIAL (SM),
LIVER (LI), LN, MESENTFRIC (MS), MAMMARY GLAND (MS), MAND SALIVARY SI, (SS), MARKOTA, STENIM (RE), SKIN (SK),
NERUE, SCIATIC (SN), DUARY (DU), PANCREAS (PA), PARRATHYROLD (PT), PITULIARY (PI), RECTUM (RE), SKIN (SK),
SPLEEN (SP), STOMACH, GL (SI), STOMACH, NONGL (SID), THYROLD (TY), TRACISCA (LD), BRIDGER SI GENDER (SP) FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATIONS 표

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STIMY PRINTEIN) WENT SAUFD ***

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/TOX SYSTEM DUTPHT *** APPENDIX 8

PRINTFO: 19-MAY-RE PAISE: 369

INDIVIDUAL ANIMAL SUMMARY REPORT

STHEP NUMBER: 2399118

SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE PATHOLOGIST: SID JONES, DUM, PHD, DACUP STUDY WEEK OF DEATH: 14 · PROSECTOR: DOUGLAS HERMOON DOSE GROUP: 4 STUDY DAY OF DEATH: 96 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL DATE AND TIME OF NECROPSY: 07/15/86 9:45 DATE OF DEATH: 07/15/86 ANIMAL NUMBER: 808509

RECORDER: SID JONES, DUM, PHD, DECUP WEIGHER: NOT REQUIRED BY PROTOCOS 227.0 GRAMS TERMINAL BODY WEIGHT:

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

YEIGHTHAUTH . CURS CLB : JEJUNUM PATHOLOGY OBSERVATIONS -ELECTRON MICROSCOPY SAMPLE; LIVER NOTE: FXTERNAL TRSERUATIONS: NOTE: GENERAL INFORMATION (XX) : *COLLECTED/TAKEN (XW) : CLINICAL OBSERVATIONS -APPEARED NORMAL

VSECTION EXAMINED; ILSSUE NOT PRESENT INFILTRATION, LYMPHOID, -SI 1841 - PERTORNALIA ZERRIVASIALAR, -DILATATION, -MODERATE PARATHYMUD (PT): VINDER MISSIRE (3E) UTFRES OFF:

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDILLA (AM), AORIA, THORACIC (AU), BONE, FFMUR (FF), BONE, STERNUM (SR),

BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),

DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HI), JI,FUM (LI), JEANUM (DE), KIDNEY (KD), FATURAL (FID), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GLOSS, MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NFRUE, SCIATIC (SN), NUARY (NU), PANCREAS (FG), PARATHYRRID (PT), PITULIARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NINGEL (SD), THYMUS (TH), THYROID (TY), TRACHER (TR), DRINARY BLADDER (DB), DTFRUS (HI)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AUNTA, THORACIC (AD), BINNE, FEMINR (FE), BONNE, STERNIM (SB),
BRAIN WASTEM (BR), CECUM (CE), COLON (CO), COND, CRRUTCAL (CS), COND, LIMMAR (LC), COND, THORACIS (ES), EYE (EY), HEART (HT), ILEUM (IL), KIDNEY (KD), LACRIMAL GL, EXO (ED), LIVER (LD),
LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARGHIM, STERBHM (GF), MISCIF, SKIEFTAL (SM),
NERUE, SCIATIC (SN), DUARY (DV), PANCREAS (PA), PITULIARY (PI), RECTUM (RE), SKIN (SK), SPLEFN (SP),
STOMACH, GL (ST), STOMACH, NONGL (SU), THYMIS (TH), THYRRID (LY), TRACHER (TR), BICHBARY RECTURE (TR)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

APPENDIX 8 *** PATHZIDX SYSTEM CHITPHT *** SUBCHRONIC TOXICITY STUDY IN RATS

PRINTFO: 12-MAY-88 PAISE: 370

INDIVIDUAL ANIMAL SUMMARY REPURT

PAINE: 5/8

STHEY NUMBER: 2399108

RECHADER: SID JUNES, DOM, PHD, DATUP WEIGHER: NIT REGULRED BY PROTOTOL 211.9 GRAMS NUP: 4 SACRIFICE STATUS! SCHEDULED, TERMINAL SACRIFICE STUDY WEEK OF DEATH: 14 TERMINAL BIDY METCHET. PATHOLOGIST: SID JONES, DUM, PHD, DACUP PRESECTOR: BARBARA DAY DOSE GRIUP: 4 STUDY DAY OF DEATH: 96 POST-FIX WEIGHER: NOT RECOURED BY PROTOCOL DATE AND TIME OF NECROPSY: 07/15/86 11:02 SEX: FEMALE DATE OF DEATH: 07/15/86 ANIMAL NUMBER: 808510

*** ANIMAL HAS NO DRGAN WEIGHTS RECORDED ***

LEGGT OF MORENING FAR CELLS, -MINING THE ILTRALIGING, LYMPHOLD, - SELIGHT -PERTBRONCHTAL ZPFRTUASCIM AR HISTOPATHOLOGY -DILATATION,-MODERATE UTERUS (UT) : LIUER (1.1) CING CLU OBSERUATIONS -ELECTRON MICROSCOPY SAMPLE; LIVER >NOTE:>EXTERNAL OBSERVATIONS:NONE -LIMEN, FLILD; BOTH HORNS, DIESR GENERAL INFORMATION (XX) : NECROPSY ^COLLECTED/TAKEN (XW) : PATHOLOGY UTERUS (UT): THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY: CLINICAL OBSERVATIONS -APPEARED NORMAL

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRIA, THURACIC (AD), RONE, FEMIN (FE), BONE, STERRUM (SB), BRAIN WYSTEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC), DUDDENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HI), ILFIM (II), BENINHUM (DF), KIDNEY (KD), LAGRIMAN G, EXO (ER), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NFRUE, SCIATIC (SM), FUNARY (FU), PANCREAC (FA), PARATHYRELD (PT), PITULIARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), SIDMACH, GL (ST), STDMACH, NINGR (SH), THYMUS (TH), THYROID (TY), TRACHEA (TR), URIMARY BLADDFR (LB)

ADRENAL, CORTEX (AC), ADRENAL, MEDILLA (AM), AIRTA, THURACIE (AD), BUBE, FEMIR (FE), BUBE, STEURIM CRD),
BRAIN LASTEM (BR), CECUM (CE), COLON (CO), CORO, CERUICAL (CS), CORO, LUMBAR (LC), CORO, THURACIE (TC),
BURDENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILFUM (H), JEJUNUM (JE), KIDNIY (KO), LARRIMA RI, FYO (TD),
LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIUARY GL (SG), MARROM, STERNUM (SE), MISCLE, SKELFTAL (SM),
NERUE, SCIATIC (SN), DUARY (DU), PANEMEAS (PA), PARATHYROND (HT), POINTIANY (PI), SFETUM (ME), SKIN (SK),
SPLEEN (SP), STOMACH, GL (SI), STOMACH, NONGL (SU), THYMUS (TH), THYROND (TY), TRACHEA (TR), (BRIMARY BI ADDIFR (HD) FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: 呈

^{***} ALL DRGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STIMY PROTOCAL) WERE SAVED ***

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/TICK SYSTEM CLUTPLIT *** APPENDIX 8

PRINTED: 12-MAY-RR PAGF: 371

STRIPY NUMBER: 24991118

INDIVIDUAL ANIMAL SUMMARY REPTIRT

TERMINAL BROY WEIGHT: 242.2 GRAMS RECYRDER: SID RWES, DUM, PHD, DACUP METGHER: NOT REQUIRED BY PRUTING SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE PATHOLOGIST: SID JONES, DUM, PHD, DACUP STUDY WEFK OF DEATH: 14 PROSECTOR: DONG AS HERNOON DOSE GRIUP: 4 STIJDY DAY OF DEATH: 96 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL DATE AND TIME OF NECROPSY: 07/15/86 12:00 SEX: FEMALE DATE OF DEATH: 07/15/86 ANIMAL NUMBER: B08511

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

INFILTRATION, LYMPHOTO, -SETGHT -PERTIRONOMENTAL /PERTUASION AR HISTOPATHON DISY LUNG CLUD : OBSERUATIONS -ELECTRON MICROSCOPY SAMPLE; LIUFR MOTEL SEXTERNAL OBSERVATIONS INCHE GENERAL INFORMATION (XX) : NECROPSY *COLLECTED/TAKEN (XW) : PATHOLOGY CLINICAL OBSERVATIONS

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AD), BONE, FEMUR (FE), BONE, STERNIM (SB),
BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORD, CFRUICAL (CS), CORD, LIMBAR (LC), CORD, THORACIC (TC),
DUDDENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), KIONEY (KD), LACRIMAL GL, EXO (ED),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), ILING (LD), MAMMARY GLAD, MAKE SALVARY GLOS, MAKEY GLOS, MUSCLE, SKELETAL (SM), NERVE, SCIATIC (SN), QUARY (QU), PANCREAS (PA), PARATHYROID (PT),
PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN (SK), CHIPER (SS), SPIFFN (SP), STUMBACH, GLOST), STUMBACH, GLOST), THYMUS (TH), THYMUS (TH), THYMUS (TH), THYMUS (TH), THYMUS (TH), THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRIA, THORACIC (AD), BUNE, FEMINE (FE), BONE, STERNUM (SB),
BRAIN WASTEM (AR), CECUM (CE), COLON (CD), CORD, CERVICAL (CS), CORD, LIMBAR (CD), CORD, THORACIC (TC),
DUDDENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEDUNUM (DE), KIDNEY (KD), LACRIMAN GI, EXD (FD),
LIVER (LI), LN, MESENTERIC (MS), MAMMARY GLAND (MS), MAND SALIVARY (3 (CB), MARKHA, STERNUM (SE), MISCUE, SKIETTAL (SM),
NERUE, SCIATIC (SN), DUARY (DU), PANCREAS (PA), PARATHYROID (PI), PITULTARY (PI), RECTUM (RF), SKIEN (SK), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGE (SID), THYMUS (TH), THYMOLD (TY), TRACHEA (TR), URIDARY MARKER (183), FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCIPTIC FXAMINATION: 뿔

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOKOL) WERE SAVED ***

APPENDIX 8 *** PATH/IDX SYSTFM CHITPHI *** SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 19-MAY-BE

INDIVIDUAL ANIMAL SUMMARY REPURT

STUDY NUMBER: 2399148

SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE DE DEATH: 14 TERMINAL BODY WEIGHT: 245.8 GRAMS C RECORDER: SID JONES, DUM, PUD, DAUNE	ACUP WEIGHER: NOT REQUIRED BY PROTOCOL
GROIUP: 4 STUDY WEEK (TOR: BARFARA DAY	PATHOLOGIST: SID JONES, DUM, PHD, DACUP
ANIMAL NUMBER: B08512 SEX: FEMALE DATE OF DEATH: 07/16/86 STUDY DAY OF DEATH: 97 DATE AND TIME OF NECROPSY: 07/16/86 9:45 PRINSEC	POST-FIX WEIGHER: NOT REDJIRED BY PROTOCOL

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

CLINICAL DBSERVATIONS	PATHOLOGY OBSERUALLONS NECROPSY	HISTOPATHOLOGY
APPEARED NORMAL	COLLECTED/TAKEN (XW): -ELECTRON MICROSCOPY SAMPLE; 1 LUFR GENERAL INFORMATION (XX): >NOTE:>EXTERNAL OBSFRUATIONS:NOWE	KIDNEY (KD): -HEPLEGIFATHY, CHRONIC PROGRESSIVE,- MINIMAL -HERS (11): -PERTBRONCHIAL/PERTVASCUL AR, INFLETRATION, LYMPHOID;-SLIGHT MANMARY HEARD (MS): >TISSUE MISSING
THE FOLLOWING ORGANS WERE LINREMARKABLE AT	T NECROPSY:	

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AD), BONE, FEMUR (FE), BINNE, STERNUM (SB),
BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CARD, CERUITAL (CS), CORD, LIMBAR-(LC), CORD, THORACIC (TO),
DUDDENUM (DB), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEDUNUM (JE), KIDNEY (KO), LACRIMAL GI, EXD (ED),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LING (LU), MAMMARY GIARD (MS), MARID SALIVARY (SS),
MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERUE, SCIATIC (SN), QUARY (DU), PARCREAS (PA), PARATHYROID (PT),
PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN (SK), SKIN (SK), SKIN (SK), URINARY BLADDER (UR), UTERUS (UI)

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ANRIA, THURACIC (AD), BUNE, FEMIR (EC), BUNE, STERNUM (SR),
BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORO, CERUTAL (CS), CORO, THURBAR (LC), CRUM, THURACIC (TC),
DUDDENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJUNUM (JE), LACRIMAL GL, EXIL (ED), LIVER (LJ),
LN, MESENTERIC (MS), MAND SALIVARY GL (SG), MARROM, STERNUM (SE), MISCLE, SKELETAL (SM), NERUE, SCHATTE (SN),
DOARY (DU), PANCREAS (PA), PARATHYROID (PT), PITHITARY (PI), NFCHIM (LS), SKLH (SR), SPECTA (SP), STUMBEL, SI (SI),
STOMACH, NONGL (SU), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (UB), UTFRUS (UT) FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: 뿔

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STIMY PRITOCOL) WFRE SAVED ***

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/TOX SYSTEM QUIPUT *** APPENDIX 8

PRINTED: 12-MAY-88

INDIVIDUAL ANIMAL SUMMARY REPORT

STUDY NIMBER: 2399108

SACRIFICE TERMINAL BODY METCHT: SACRIFICE STATUS: SCHEDIER, FROMINAL PATHOLOGIST: SID JONES, DUM, PHD, DAIJUP STUDY WFEK OF DEATH: 14 PROSECTOR: BARBARA DAY DOSE GROUP: 4 STUDY DAY OF DEATH: 97 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL DATE AND TIME OF NECROPSY: 07/16/86 11:04 SEX: FEMALE DATE OF DEATH: 07/16/86 ANIMAL NUMBER: B08513

RECHEDER: SID JUNES, DUM, PHD, DACUP WEIGHER: NOT REQUIRED BY PROTOCOL 236.4 GRAMS

*** ANIMAL HAS NO DRGAN WEIGHTS RECORDED ***

CLINICAL OBSERVATIONS	PATHOLOGY DRSERVATIONS NECROPSY .	PATHOLOGY DBSERVATIONS HISTOPATHOLOGY NECROPSY .
SALIUATION	^COLLECTED/TAKEN (XW): -ELECTRON MICROSCOPY SAMPLE; LIUFR GENERAL INFORMATION (XX); >MOTE:>EXTERMAL MRSFRUATIONS:SALIUATION	LIVER (L.1) : -FOCT THE MORTHURD FAR CELLS,-MINIMAL LUNG (L.U) : -FERTHERINGH ALZERTUASCHERR, INFLITRATION, LYMPHOLO,-MINIMAL >TISSHE MISSING

DRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRIA, THORACIC (AD), BONE, FEMIR (FE), BONE, STERNIM (SB),
BRAIN WASTEM (BR), CECUM (CE), COLON (CD), CHRO, CERVICAL (CS), CHRO, LIMBAR (LC), CHRO, THORACIC (TC),
DUDDENUM (DU), ESOPHABUS (ES), EYE (EY), HEART (HT), ILEUM (IL), DEJUNIM (JE), KIDNEY (KO), LACRIMAL GL, EXD (ED),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LING (LU), MAMMARY GLAD (MS), MAND SALIDARY GLOS, MAND SALIDARY GLOS, MAND SALIDARY GLOS, MAND SALIDARY GLOS, PARATHYROLD (PT),
PITUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPLEFN (SP), STOMACH, GLOST), STOMACH, GLOST, STOMACH, GLOST), THYMUS (TH), THYROLD (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT) THE FOLLOWING ORGANS WERE UNREMARKABLE AT MECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRTA, THDRACIC (AD), BONE, FEMIRE (FE), BONE, STERNIM (SB), BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CRED, CECUM (CE), COLON (CO), CRED, LACRIMAL GL, EXO (ED), DUDOENUM (DD), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEJONNIM (JE), KIDNEY (KD), LACRIMAL GL, EXO (ED), LN, MESENTERIC (MS), MAND SALIVARY GL (SG), MARRIM, STERNIM (SE), MISCIF, SKFIFTAL (SM), NFRUF, SCLATIC (SN), DUARY (DO), PANCREAS (PA), PARATHYROLD (PT), PITULTARY (PL), RECTUM (RE), SKIN (SK), SPLEEN (SP), STOMACH, GL (SL), INYMUS (TH), THYROLD (TY), TRACHEA (TR), HRIMARY HEADDER (HB), HIFRES (HI)) THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THF STIMY PROTOCOL) WERE SAVED ***

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/INX SYSTEM NUTPHIT *** APPENDIX 8

PRINTED: 12-MAY-8H PAGE: 374

INDJUIDIDE ANIMAL SUMMARY REPORT

STHOY MIMBER: 9399108

251.9 GRAMS TERMINAL BODY WEIGHT: 29
RECORDER: PARHARA DAY SACRIFICE STATUS: INSCREDIUED (D) PATHOLOGIST: NOT REQUIRED BY PROTOCOL STUDY WEEK OF DEATH: 11 PROSECTOR: BARBARA DAY DASE GROUP: 4 STUDY DAY OF DEATH: 71 POST-FIX WEIGHER: NOT REDUIRED BY PROTOCOL DATE AND TIME OF NECROPSY: 06/20/86 15:38 SEX: FEMALE DATE OF DEATH: 06/20/86 ANIMAL NUMBER: 808514

WEIGHER: NOT REQUIRED BY PRINTOROU

*** ANIMAL HAS NO ORSAN WEIGHTS RECORDED ***

INFILTRATION, LYMPHOID, -SELIGHT -PERTERBUTH A ZPERTUASION AR HISTOPATHOLDGY -FIRETRI MATERIAL , - PRESENT 3 PATHOLOGY NBSFRUATIONS -MOTTLED; ALL LOBES, LIGHT TO DARK RED GENERAL INFORMATION (XX): -FAILURE IN COLLAPSE; ALL LOSFS NOTE: LAST IN-LIFF AND EXTERNAL **OBSERUATIONS: NONE** NECROPSY CLINICAL OBSERVATIONS 111111111111 -APPEARED NORMAL

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRIA, THORACIC (AD), BINE, FEMUR (FE), BUNE, STERNIM (SB),
BRAIN MASTEM (BR), CECUM (CE), COLON (CD), CORD, CERVICAL (TS), CHRD, LIMBAR (LD), CORD, HORACIC (TC),
BUDDENIM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (LL), DEJUNIM (JE), KIDNEY (KD), LAFRIMAR B, EXH (ED),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), MAMMARY GLAND (MS), MAND SALIVARY GL. (SS), MARRIA, STERNIM (SF),
MUSCLE, SKELETAL (SM), NERUE, SCIATIC (SN), DUARY (DU), PANCREAS (PA), PARATHYROID (PI), PITULIARY (PI), RECTUM (RF),
SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NINGS (SH), THYRUS (TR), THYRUS (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT), ^CDLLECTED/TAKEN (XW) THE FOLLOWING ORGANS WERE INREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ABRIA, THURACIC (AU), BUNE, FEMIRE (FF), BUNE, STERNIM (SR),
BRAIN MLSTEM (BR), CECUM (CE), COLON (CD), CORD, CERVICAL (CS), CORD, LIMBAR (LC), CORD, THURACIC (TC),
BUNDENUM (DU), ESOPHAGUS (ES), FYE (EY), HEART (HT), ILEUM (1E), KEJIRH (JF), KADNEY (KD), LACETMAN HI, FYO (FU),
LIVER (LI), LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROLM, STERNIM (SF), MISCLE, SKELETAL (SM),
NERUE, SCIATIC (SN), BUARY (DU), PANICRE AS (PA), PARATHYROLD (PY), PITHILARY (PY), RECHIM (MF), SKIN (SK),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SD), THYMUS (TH), THYROLD (TY), TRACHEA (TR), URLHARY BL ADDER (HR), FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: UTERUS (LÍT) 뿣

*** ALL ORGANSZIISSUES (REGIURED IN BE HARVESTED PER THE STIDY PRITICIAL) WERE SAUED ***

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/IDX SYSTEM DUIPUT *** APPENDIX 8

PRINTED: 32-MAY-88 PAGE: 375

INDIVIDIDAL ANIMAL SUMMARY REPORT

STUDY MIMPIFEL 939914R

TERMINAL BODY WEIGHT: SACRIFICE STATUS: INSCHEDING (D) PATHOLOGIST: NOT REDUITRED BY PRITICOL STUDY WEEK OF DEATH: 2 PROSECUTIR: KIM LIMON N DOSE GROUP: 4 STUDY DAY OF DEATH: 10 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL DATE AND TIME OF NECROPSY: 04/20/86 12:00 DATE OF DEATH: 04/20/86 ANIMAL NUMBER: B08515

WEIGHER: NOT REDILIRED BY PRINCE RECORDERS KIN LINGSHIN

HISTOPATHIN DGY

-FORFIGN MATERIAL : - PRESENT

CENS (CED ::

MAMMARY IN AND (MR):

-EDEMA,-MODERATE TISSUE MISSING PARATHYROLD (PT):

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

CLINICAL OBSERVATIONS

-APPEARED NORMAL

PATHOLOGY OPSERUATIONS -FAILURE TO COLLAPSE; ALL LORES, FLUID OBSERVATIONS ANIMAL WENT INTO A FULL CONVILSION AND DIED SEVERAL NUTER LAST IN-LIFE AND EXTERNAL GENERAL INFORMATION (XX): NECROPSY -MOTTLED; ALL LIBES

SECTION EXAMINED, TISSUF NOT PRESENT

MUSCLE, SKELETAL (SM), NERUE, SCHATIC (SN), QUARY (QU), PANCREAS (PA), PARATHYROID (PT), PITLITTARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STUMACH, RLUAG (SD), THYMUS (TH), THYROID (TY), ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORTA, THORACIC (AD), BONE, FEMUR (FE), BONE, STERMIM (SR), BRAIN W/STEM (BR), CECUM (CE), COLON (CD), CORD, CERVICAL (CS), COLON (CD), CORD, THORACIC (TC), DUDDENUM (DV), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), DEJUNUM (DF), KIONEY (KD), LACRIMAL GI, EXO (FO), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), MAMMARY GIAND (MS), MAND SALIVARY GI (SS), MARRIL, STERNIM (SF), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT), ACOLLECTED/TAKEN (XW) THE FOLLOWING ORGANS WERE LINREMARKABLE AT NFCROPSY:

MINITES AFTER GAURICE DISTRIC

!

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AORIA, THORACIC (AD), BONE, FEMIR (FE), FONE, SIGRAH COR),
BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TN),
DUDDENUM (DU), ESOPHAGUS (FS), EYE (EY), HEART (HI), ILEIM (RI), ALDIBER (LC), KIDBEY (RD), LAGRIMAL GI, SOL
LIVER (LI), LN, MESENTERIC (MS), MAND SALIVARY GL (SG), MARROW, STERNIM (SE), MISCLE, SKELETAL (SM),
NERUE, SCIATIC (SN), DUARY (DU), PANCREAS (PA), PITUITARY (PI), RECIEM (RE), SKIR (SO), ADLER (SP),
STOMACH, GL (ST), STOMACH, NONGL (SD), THYMUS (TH), THYROLD (TY), TRACHEA (TR), LIRINARY BLADDER (1R), UTERES (11) THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

APPENDIX B *** PATH/IOX SYSIFM QUIPUT *** SUBCHRONIC TOXICITY STUDY IN RAIS

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INDIVIDUAL ANIMAL SUMMARY REPORT

12-MAY-1	<u> </u>
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PRINTED:	Police

STHEY NEMBER: 2399188

ORGAN NAME ORGAN WE ORGAN W	ORGAN WEIGHT			
(BR) 2	(GRAMS)	ORGAN WEIGHT RELATIVE TO RODY WEIGHT (%)	DRGAN TO BRAIN METCHT RATIO	0 R G A N S T A T U S
(BR) 2	.076	, 1086 %	0820.	WEIGHT TAKEN
(SP) (SP) (CL1)	2,05	% 977. % 747.	1.888	METCHT TAKEN METCHT TAKEN
(KD) 2	.61	2 元//·	666	-
(L1)	2.11	× 962.	1.028	
*	9.n1	3.397 %	4,386	UF 1831 TAKEN
CLINICAL OBSERVATIONS	Z Z Z Z Z Z Z Z Z Z Z Z Z Z Z Z Z Z Z	OBSERUATI ECROPSY	G R C	HISTOPATHOLOGY
-APPEARED NORMAL	CECUM (CE): -DARK AREA; IN 1.0 X 0.5 CM >NOTE:>DARK ARE SITE UTERUS (UT): -LUMEN, FLUID; GENERAL INFORMATIO	CECUM (CE): -DARK AREA; IN WALL, UNE, DACK RED, 1.0 X 0.5 CM >NOTE: DARK AREA, POSSIBLE INJECTION SITE UTERUS (UT): -LUMEN, FLUID; BOTH HORNS, CLEAR GENERAL INFORMATION (XX): >NOTE: >FXTFRHAL ORSERVATIONS: NUTE		CUM (CE): OTHER MARKARE F VER (LT): -FOCT OF MONDMEDLEAR CELLS,-MINIMAL -PERTBRONCHIAL/PERTVASCULAR; TNFILTRATION, LYMPHOTO,-MINIMAL -FRUS (UT): -DISTIBUTE ATTENTION - LYMPHOTO - MINIMAL -DISTIBUTE - MIDERATE Y SEVERE

APPENDIX 8 *** PATH/IIIX SYSTEM DUTPUT *** SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-88

INDIVIDUAL ANIMAL SUMMARY REPORT

STHINY NUMBER: 2399108

TERMINAL BRDY MEIGHF: 265.2 GRAMS RECORDER: SID HOMES, DUM, PUD, DATUP 265.2 GRAMS SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE WETGHER: DINIBLAS HERMOTH PATHOLOGIST: SID JONES, DUM, PHD, DACUP STIMY WEEK OF DEATH: 14 PROSECTOR: DOLIGIAS HERNDON DUSE GROUP: 4 DATE OF DEATH: 07/15/86 STUDY DAY OF DEATH: 96
DATE AND TIME OF NECROPSY: 07/15/86 14:14
PRINSE POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL ANIMAL NUMBER: B08516 DATE OF DEATH: 07/15/86

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDILLA (AM), ADRIA, THORACIC (AD), BOBE, FFMIR (FF), ROBE, SIFRNIM (SB),

BRAIN WASTEM (BR), COLON (CD), CORD, CERUICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC), DIODENUM (DB),

ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), DEDINNIM (DE), KIDNEY (KD), LACRIMAL (B, FXO (FD), 1104R (L)),

LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNIM (SF),

MUSCLE, SKELETAL (SM), NERUE, SCIATIC (SN), DOARY (CN), PANCHEAS (PA), PARATHYROLD (PT), PITHITARY (PT),

SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), THYMUS (TH), THYROLD (TY),

TRACHEA (TR), URINARY BLADDER (LB), ^COLLECTED/TAKEN (XM)

ADRENAL, CORTEX (AC), ADRENAL, MEDILLA (AM), ADRIA, THORACIC (AD), BIRME, FFMIR (FE), BIRME, SIFRNIM (SR),
BRAIN MASTEM (BR), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC), DINDEMIM (DI),
ESOPHAGUS (ES), EYE (EY), HEART (HI), ILEUM (IL), JEJUNIM (JE), KIDMEY (KD), LAGRIMAL A, FXO (ED),
LN, MESENTERIC (MS), MANMARY GLAND (MG), MAND SALIVARY GL (SG), MARROM, STERNIM (SE), MUSCLE, SKELETAL (SM),
NENUE, SCIATIC (SN), DUARY (DU), PANCREAS (PA), PARATHYROLD (PT), PITHITARY (PI), RESTUM (NF), SKIN (SK),
SPLEEN (SP), STOMACH, GL (SI), STOMACH, NONGL (SU), THYMUS (TH), THYROLD (TY), TRACHEA (TR), URINARY BI ADDER (18) THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

A** PATH/TOX SYSTEM DUTPUT *** SUBCHRONIC TOXICITY STUDY IN RATS

FRINIFU: 12-MAY-BE PAGE: 378

INDIVIDUAL ANIMAL SUMMARY REPORT

SUMMARY REPORT STUDY NUMBER: 2399108

ANIMAL NUMBER: 808517 SEX: FEMALE DOSE DATE OF DEATH: 07/15/86 STUDY DAY OF DEATH: 96 DATE AND TIME OF NECROPSY: 07/15/86 14:51 PROSECT POST-FIX WEIGHER: NOT REQUIRED BY PROTOCO!. PATHOLO	SEX: FEMALE DOSE GI STUDY DAY OF DEATH: 96 715786 14:51 PROSECTION D BY PROTOCOM. PATHOLOG	DOSE GROUP: 4 SACRIFICE STATUS: 1: 94 STUDY WEEK OF DEATH: 14 PROSECTOR: BARBARA DAY PATHOLOGIST: SID JONES, DUM, PHD, DACUP	SCHF TERM	SCHFOURED, TERMINAL SACRIFICE TERMINAL BODY WEIGHT: 223.0 GRAMS RECORDER: SID JONES, DUM, PUD, DACUP WEIGHFR: BARBARA DAY
ORGAN MAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO BODY WEIGHT (%)	ORGAN TO BRAIN METISHT RATHII	ORGAN STATES
ADRENAL (AD)	720.	. 0345 %	500 C	LEIGHT TAKEN
DUARY (DU) BRAIN W/STEM (BR)	2.07	. 0525 . 928 . 928	. 0565 1. ຕສດ	WEIGHT TAKEN WEIGHT TAKEN
HEART (HT)	.70	.314 %	.338	WEIGHT TAKEN
SPLEEN (SP)	. 48	.215 %	326*	DETCH TOKEN
KIDNEY (KD)	1.96	8 628	.947	ME IGHT TAKEN
LIVER (LI)	8.25	3,700 %	3.98A	METCHT TOKEN
CLINICAL OBSERVATIONS		ATHOLOGY OBSERUATIONS NECROPSY	S Z C	HISTOPATHOL NGY
-APPEARED NORMAL	GENERAL INFO	GENERAL INFORMATION (XX): >MOTE:>FXTERNAL (ABSFRUATIONS:NIME	LUNG (LU) : -PERTERUM INFILTRATE	ING (LU): -PERIBRAHAL/PERIVASHALAR, INFILTRATION, LYMPHOID,-SLIGHT

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/INX SYSTEM GITPHT *** APPENDIX 8

PRINTFU: 19-MAY-88

THDIVIDUAL ANIMAL SHMMARY REPORT

STIBY NIMBER: 9399148

RECERPTES SID JONES, DUM, PID, DATUP TERMINAL BODY WEIGHT: 223.0 GRAMS SACRIFICE WETGHFR: BARBARA DAY SACRIFICE STATUS: SCHEDULED, TERMINAL PATHOLOGIST: SID JONES, DUM, PHO, DACUP STUDY WEEK OF DEATH: 14 PROSECTOR: HARBARA DAY DOSE GROUP: 4 STUDY DAY OF DEATH: 96 POST-FIX WEIGHER: NOT REGUIRED BY PROTOCOL SEX: FEMALE DATE AND TIME OF NECROPSY: 07/15/86 14:51 DATE OF DEATH: 07/15/86 ANIMAL NUMBER: B08517

THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AGRIA, IHORACIC (AN), ROWF, FFMIR (FE), BONF, STERNIM (SB), BRAIN WZSTEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC), DUDDENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HI), ILEIM (IL), AFIRMIM (AE), KIDNEY (KD), LAGRIMAL GI, EXO (ED), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUNG (LU), MAMMARY GLAND (MS), MAND SALIUARY G. (SG), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NERUE, SCIATIC (SM), DUARY (DU), PARATIRES (PA), PARATIRETHD (FT), PILUITARY (PI), RECTUM (RE), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STIMACH, G. (ST), STIMACH, NINGS (SH), THYROLD (TY), TRACHEA (TR), HRINARY BLADDER (1B), HIFRES (HI), ACHLEDZIACH (XW)

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AN), ADRIA, THORACIC (AL), BIDNE, FEMINE (EE), BURE, STERNIM (SB),
BRAIN WASTEM (BR), CECUM (CE), COLON (CD), CORD, CERVIDAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC),
BUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HI), ILENM (HI), ALINNIM (DI), LADREY (KD), LADRINAL RI, EXC. (ET),
LIVER (LI), LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIVARY GL (SG), MARROW, STERNIM (SF), MISCLE, SKFLETAL (SM),
NERUE, SCIATIC (SN), DUARY (DU), PANCREAS (PA), PARATHYROID (PI), PITHITARY (PI), RECTUM (RF), SKIN (SK),
SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SN), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BIADDER (18), UTERUS (UT)

*** ALE ORGANS/TISSNES (REQUIRED TO BE HARVESTED PER THE STHOY PROTOKEN) WERE SAUFD ***

APPENDIX 8 *** PATH/TOX SYSTEM DUTENIT *** SUBCHRONIC TOXICITY STUDY IN RATS

PRINTED: 12-MAY-RS PAGE: 380

STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

ANIMAL NUMBER: B08518, SEX: FEMALE DATE OF DEATH: 07/16/86 STUDY DAY OF DATE AND TIME OF NECROPSY: 07/16/86 10:30 PRST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL	DEATH	DOSE GROUP: 4 SALKHE HT STATUST SCHEDMINT, TENNING, SALKETTER 13-7 STUDY WEEK OF DEATH: 14 TERMINAL BODY WEIGHT: 239.8 PROSECTOR: TIM GROUE RETAINED BODY WEIGHES, DUM, PHD, DACUP WEIGHER: SID JONES, DUM, PHD, DACUP WEIGHER: TIM GROUE	TERM	TERMINAL BODY WEIGHT: 239.8 GRAMS RECHROFR: SID HOMES, DUM, PHD, DACUP WEIGHER: TIM GRIVE
ORGAN NAME	ABSOLUTE ORGAN WEIGHT (GRAMS)	ORGAN WEIGHT RELATIVE TO PROY WEIGHT (%)	ORGAN TO BRAIN METGHT RATITI	0 R G A K S 1 A T H S
ANDENO: COD.	G 90	1094 %	. 4362	LIFTIGHT TAKEN
DOMESTIC COLD	. 115	.0480	. 0612	WEIGHT TAKEN
BRAIN MASTER (BR)	1.88	28.4 %	1.000	WE HANT TRKEN
HEART (HT)	. 22	.321 %	.410	WFIGHT TAKEN
SPIEEN (SP)	53	第 「200'·	282.	LIFT TAKEN
KIDNEY (KD)	1.88	78.4 %	1.060	MFIGHT TAKEN
LIVER (L1)	7.73	3.924 %	4.112	NEWS LESS STREET
CLINICAL OBSERVATIONS	PATHOL	THOLOGY ORSERVATIONS NECROPSY	S 7 C	HISTOPATHOLOGY
-APPEARED NORMAL	GENERAL INFORM	GENERAL INFORMATION (XX): >NOTE:>EXTERNAL DRSFRUATIONS:NOHE	LING (LI):	NG (LID): IPERISEMENTAL ZERTUGGIJI AR, INFILTRATION, LYMPHOTO,-SCIENT

APPENDIX 8 *** PATH/IOX SYSTFM CHITPUT *** SUBCHRONIC TOXICITY STEDY IN RAIS

PRINTED: 12-MAY-80 PARE: 381

INDIVIDUAL ANIMAL SIMMARY REPORT

BILLOSEG SALBBURN KONTES

RELORDER: SID JONES, DUM, PHD, DACUP 239.8 GRAMS SACRIFICE STATUS: SCHEDULFO, TERMINAL SACRIFICÉ TERMINAL BODY WFIGHT: WEIGHER: TIM GRADE PATHOLOGIST: SID JONES, DUM, PHD, DACUP STIJDY WEEK OF DEATH: 14 PROSECTOR: TIM GROVE DIISE GRIMP: 4 STUDY DAY OF DEATH: 97 POST-FIX WEIGHER: NOT REDUIRED BY PROTOCOL DATE AND TIME OF NECROPSY: 07/16/86 10:30 SEX: FEMALE DATE OF DEATH: 07/16/86 ANIMAL NUMBER: BOB518

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AIRTA, THORACIC (AD), PURE, FFMIR (FE), BURE, STERMUM (SB), BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORD, CORD, LUMBAR (LC), CORD, THORACIC (TC), DUDDENUM (OU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILFIM (TL), LUMBAR (LC), KIDMEY (KO), LATRIMAL IN, FAN (FD), LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), LUMB (LJ), MAMMARY GLAND (MG), MAND SALIDARY G. (SG), MASCLE, SKELETAL (SM), NERUE, SCIATIC (SN), (WARY (HD), PARTREAS (PA), PARTREAS (PA), PARTREAS (PA), PARTREAS (PA), FARACHTO (RE), SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STUMACH, GL (ST), STOMACH, NINGL (SD), THYMUS (TH), THYROID (TY), TRACHEA (TR), HRINARY BLADDER (1R), HTFRIS (HT), ACTUTECTED/TAKIN (XM) THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRIA, THORACIC (AD), ROWE, FEMIR (FE), BOWE, SIFRNUM (SE),

BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LIMBAR (LC), CORD, THORACIC (TC),

BRAIN WASTEM (BR), CECUM (CE), EYE (EY), HEART (HT), ILFUM (IL), NFURMUM (DE), KIDNEY (KD), LAGRIMAH (E),

CHOREN (LI), LN, MESENTERIC (MS), MAMMARY GLAND (MG), MAND SALIUARY GL (SG), MARROW, STERNUM (SE), MISCLE, SKFLETAL (SM),

NERUE, SCIATIC (SN), RUARY (DU), PANCREAS (PA), PARATHYROID (PT), PITHIDAKY (PT), RECTUM (RE), SKIN (SK),

SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SU), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (18),

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PFR THE STIMY PRINTINI)) WERF SAVED ***

*** PATH/TOX SYSTEM QUIPUT *** APPENDIX 8

SUBCHRONIC TOXICITY STUDY IN RATS

PRINTFD: 12-MAY-88

STUDY NUMBER: 2399108

INDIVIDUAL ANIMAL SUMMARY REPORT

RECORDER: SID JONES, DUM, PHD, DACUP 284.1 GRAMS SACRIFICE STATUS: SCHEDULED, TERMINAL SACRIFICE TERMINAL PINCY DETICHT:

LIFTGHER: ANT REMITRED BY PROTOSOM PATHOLOGIST: SID JANES, DUM, PHD, DACUP STRIPY LIFFK OF DIATH: 14 PROSECTOR: DOLIGLAS HERNDON DOSE GROUP: 4 SEX: FEMALE STUDY DAY OF DEATH: 97 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL DATE AND TIME OF NECROPSY: 07/16/86 11:55 DATE OF DEATH: 07/16/86 ANIMAL NUMBER: B08519

*** ANIMAL HAS NO DRGAN WEIGHTS RECORDED ***

	PATHOLOGY RRSERUATIONS	
CLINICAL OBSERUATIONS	NECROPSY	HISTOPATHIN DGY
-APPEARED NORMAL	COLLECTED/TAKEN (XW): -ELECTED/TAKEN (XW): -ELECTED/TAKEN MICROSCINEY F; 1 TOFR GENERAL INFORMATION (XX): >NINTE:>EXTERNAL ORSFRUATIONS:NIBIF	LIVER (LT): -FORT OF MORRHALL FOR CELLS, -SLIBHT LUNG (LU): -PERTERNALHALZPERIVASCULOR, INFILTRATION, LYMPHOLD, -SLIGHT
THE END OPCOME STATE OF THE FIRST NECTOR STATES AT METERS AND SAFETY OF THE FIRST NECTOR STATES AT METERS AND SAFETY OF THE PROPERTY OF THE PR	AT NECROPOSY:	

FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:
ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRENAL, CORTEX (EC), FORES, STERNIM (SB),
BRAIN W/STEM (BR), CECUM (CE), COLLON (CO), CORO, ESPUTEDA (LC), CORO, THORAGIC (TC),
BRAIN W/STEM (BR), CECUM (CE), COLLON (CO), CORO, CERVICAL (CS), CORO, CERVICAL (CS), ADIRENA (AL), KIDNEY (KD), LATENEY (KD), LATENEY (KD), LATENEY (CO), BAND SALIVARY (B (SB), FXM (FN), LUMS (LU), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NFRUE, SCIATIC (SM), MARROW, STERNUM (SE), MUSCLE, SKELETAL (SM), NFRUE, SCIATIC (SP), STOWACH, GL (ST), STOMACH, MONG! (SD),
THYMUS (TH), THYROID (TY), TRACHEA (TR), HRINARY BLADDER (HB), HTFRIS (HT)

DUDDENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), DEUM (LL), JEJUNEM (JE), KIDNEY (KD), LATRIMAL H, EXECTEL (SE), MARSON, STERNIM (SE), MISCLE, SKELETAL (SE), NERVE, SCIATIC (SN), NOARY (DU), PANCREAS (PA), PARATHYRIDO (PT), PLUIDARY (PL), RECIEM (RE), SKIH (SK), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NORICL (SU), THYMUS (TH), THYROID (TY), TRACHEA (TR), URINARY BLADDER (18), ADREMAL, CORTEX (AC), ADREMAL, MEDULLA (AM), ADRIA, THORACTC (AD), PONE, FEMIRE (FC), ROBE, STERBUM (CB), BRAIN WYSTEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACTC (TC), THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: UTERUS (UT)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PRUTOCOLD WIRE SAUCH) ***

APPENDIX 8 *** PATH/TOX SYSTEM DUTPUT *** SHBCHRONIC TOXICITY STIDY IN RAIS

PRINTED: 12-MaY-88 PASE: 383

INDIVIDUAL ANIMAL SUMMARY REPORT

STHOY NEMBER: 2399118

TERMINAL BRINY JETICHT: 214.2 GRAMS RECORDER: BARBARA DAY JETICHER: MAT REGIUEED HY PROTOENT SACRIFICE STATUS: UNSCHEDULED (D) PATHOLOGIST: MIT REQUIRED BY PROTOGOL STEDY WEEK OF DEATH: 7 PROSECTOR: BARBARA DAY DOSE GROUP: 4 SEX: FEMALE DOS STUDY DAY OF DEATH: 49 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL DATE OF DEATH: 05/29/86 STUDY DAY OF DATE AND TIME OF NECROPSY: 05/29/86 11:05 ANIMAL NUMBER: 808520

***, ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

-APPEARED NORMAL

HISTOPATHOLOGY DINDENNIM (DIN : arathana (ara) : ILEUM (11.) COLON (CO) : CECUM (CF) : SHIIDI YIIC SPRING YILC SPRITTLY YILD MAINTON YTIC **MALITOLYTIC** PATHOLOGY OBSERVATIONS -MOTTLED; ALL LOBES, LIGHT TO DARK RED OBSERVATITINS: DARK RFD FLIID -FAILURE TO COLLAPSE; ALL LORES NOTE: > LAST IN-LIFE AND EXTERNAL GENERAL INFORMATION (XX) : SURROUNDING NARES NECROPSY LUNG (LU): CLINICAL DBSERVATIONS

-FIRETGN MATERIAL, -PRESENT

-FDERA, - MIDFRAIF

RECTUM (RE) :

CALLEY YELL

SUBCHRONIC TOXICITY STUDY IN RATS *** THRING MYTSYS XOTANDER *** APPENDIX B

PRINIFIN: 12-MAY-88

INDIVIDUAL ANIMAL SUMMARY REPORT

SU16666 ** PRIMININI YOURS

•	,				
ANIMAL NIMBER: B08520	SEX: FEMALE	DOSE GROUP: 4	SACRIFICE STATIS: INSCHEDULED (D)	INSCHEDII FD (D)	
DATE OF DEATH: 05/29/86	STLIDY DAY OF DEATH: 49		STUDY WEEK OF DEATH: 7	TERMINAL BODY WEIGHT: 214.2 GRAN	214.2 GRAI
. DATE AND TIME OF NECROPSY: 05/29/86 11:05	05/29/86 11:05	PROSECTOR: BARBARA DAY	PAY.	RECORDERS NARBARA DAY	.₩.
POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL	IRED BY PROTOCOL	PATHOLOGIST: NOT REQUIRED BY PROTOCOL	IJIREO BY PROTOCOL	WEIGHER: NOT REDUIRED BY PRITT	RFD BY PRITE
THE METERIAL NO. 1 - 1001	ואבט מי ראטוטכטר		DIALLY OF THE COMP.		2

IC. III. THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY:

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), AMRIA, THURACIC (AM), BUNE, FEMIR (FE), BUNE, STERNEM (SB),
BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LIMBAR (LC), CORD, THORACIC (TC),
DUODENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (1F), MITHINIM (ME), KIDNEY (KD), LAGRIMAL GL, FXB (FD),
LIVER (LI), LN, MESENTERIC (MS), LN, OTHER (LN), MAMMARY GLAND (MS), MAND SALIVARY GL (SG), MARRIM, STERNUM (SF),
MISCLE, SKELETAL (SM), NERUE, SCIATIC (SN), DUARY (MV), PANERFAS (PA), PARATHYROLD (PT), PILLITARY (PT), SCILLM (RF),
SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NONGL (SD), THYMUS (TH), THYROLD (TY), TRACHER (TR), URINARY BLADDER (UB), UTFRUS (UT), "COLLECTED/TAKEN (MA)

FOILCOWING TISSUES WERE UNREMARKABLE AT MICROSCOPIC EXAMINATION: 뿔

ADRENAL, CORTEX (AC), ADRENAL, MEDILLA (AM), AORTA, THORACIC (AC), BONE, ESOPHAGIS (ES), EYE (EY), HEART (HT), BRAIN WASTEM (BR), CORD, CERVICAL (CS), CORD, LUMBAR (LC), CORD, THORACIC (TC), ESOPHAGIS (ES), EYE (EY), HEART (HT), KIDNEY (KD), LACRIMAL GL, EXO (ED), LIVER (L1), IN, MESENTERIC (MS), MAMMARRY GLAND (MS), MAND SALIVARY GLAND (MS), MUSCLE, SKELETAL (SM), NERUE, SCIATIC (SN), QUARY (QU), PANCREAS (PA), PARAIHYRHID (PT), PITULIARY (PI), SKIN (SK), SPLEEN (SP), STOMACH, GL (ST), STOMACH, NOWGL (SD), THYMUS (TD), THYRHID (TY), TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT)

*** ALL ORGANS/TISSUES (REQUIRED TO BE HARVESTED PER THE STUDY PROTOCOL) WERE SAVED ***

SUBCHRONIC TOXICITY STUDY IN RATS *** PATH/TEIX SYSTEM DUTPIT *** APPENDIX B

PRINTED: 19-MAY-8R PAGE: 385

INDIVIDUAL AHIMA SHMMARY REPURT

BILLOGG FRENCHIN YOURS

SAURTETTE STATUS: SUMFOULTD, TERMINAL PATHOLOGIST: SID JONES, DUM, PHD, DACUP STUDY WEEK OF DEATH: 14 PROSECTOR: DOLIGHAS HERNDON DOSE GROWP: 4 STUDY DAY OF DEATH: 97 POST-FIX WEIGHER: NOT REQUIRED BY PROTOCOL DATE AND TIME OF NECROPSY: 07/16/86 12:20 DATE OF DEATH: 07/16/86 ANIMAL NIMBER: B08521

TERMINAL BODY WEIGHT: 258.6 GRAMS RECERDINES, DUM, PRD, DAEDP WEIGHER: MIT REGISTRED BY PRITTIEN

*** ANIMAL HAS NO ORGAN WEIGHTS RECORDED ***

-CHRONIC INCIDENTION, NAROFRIAN SCRID, -INFILITRATION, LYMPHOLD, -SI IGHT -PERTBRONCHIAL / PERTUASION AR HISTOPATHOL OBY IN, MESENTERIC (MS) : -CONSEST FOR, -St. IGHT . SE SEC EYE (EY) PATHOLOGY OBSERVATIONS -DARK AREA; CHE, DARK RFD, 2 X 4 MM >NOTE:>DARK AREA, POSSIBLE INJECTION *COLLECTED/TAKEN (XW) : *-ELECTRON MICROSCOPY SAMPLF; | | JUFR >NOTE:>EXTERNAL OBSERUATIONS:NONE GENERAL INFORMATION (XX): NECROPSY LN, MESENTERIC (MS) : SITE THE FOLLOWING ORGANS WERE UNREMARKABLE AT NECROPSY: CLINICAL DBSERVATIONS -APPEARED NORMAL

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AM), ADRIA, THORACIC (AD), BONE, FEMUR (FE), BONE, STERNIM (SB),
BRAIN WASTEM (BR), CECUM (CE), COLON (CD), CORD, CERUITAL (CS), TORD, LUMBAR (LD), CHRD, THORACIC (TC),
DUDDENUM (DU), ESOPHAGUS (ES), EYE (EY), HEART (HT), ILEUM (IL), JEDUNUM (JE), KIDNEY (KD), LATRIMAL GI, EYE (EV),
LIVER (LI), LN, OTHER (LN), LUNG (LU), MANMARY GLAND (MG), MAND SAI JUARY (L (SG), MARKOLL, STERBEM (SF),
MUSCLE, SKELETAL (SM), NERUE, SCIATIC (SN), QUARY (QU), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), RECTUM (RF),
SKIN (SK), SKIN, OTHER (SS), SPLEEN (SP), STOMACH, GL (ST), STOMACH, MURGH (SB), HYBRIS (TD), THYROID (TY),
TRACHEA (TR), URINARY BLADDER (UB), UTERUS (UT)

ADRENAL, CORTEX (AC), ADRENAL, MEDULLA (AN), ADRIA, THORACIC (AD), BONE, FEMIR (FE), BINE, STERNIM (SR),
BRAIN WASTEM (BR), CECUM (CE), COLON (CO), CORD, CERVICAL (CS), CORD, LHORACIC (CO), TILEDM (L),
BUDDENUM (DU), ESOPHAGUS (ES), HEART (HT), ILEDM (LL), JEJUNUM (JE), KIDNEY (KD), LATRIMAL G), EXO (ED), LIVER (LL),
MANIMARY GLAND (MG), MAND SALIDARY GL (SG), MARRIM, STERNIM (SF), MISCO F, SKILETAL (SM), MICCO (CH),
DOARY (DU), PANCREAS (PA), PARATHYROID (PT), PITUITARY (PI), RECTUM (RE), SKIN (SK), SPIEFN (SP), STOMACH, GI (SD), STOMACH, NINGL (SU), THYMUS (1H), THYROID (TY), TRACHER (TR), HRINARY (LANDER (HR), HITERE (HR) THE FOLLOWING TISSUES WERE UNREMARKABLE AT MICROSCIPIC EXAMINATION:

^{***} ALL ORGANS/TISSUES (REGILIRED TO BE HARUESTED PER THE STIDY FRITIGIAL) LAFGE SAUTO ***

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APPENDIX 9

Analytical Chemistry Report



SPONSOR: DYNAMAC CORPORATION

MATERIAL: M-XYLENE (M-XYLOL) CAS 108-38-3

SUBJECT: FINAL REPORT

Subchronic Toxicity Study

m-Xylene in Corn Oil Gavage Formulations

Project No. 2399-108

1. OBJECTIVE:

The purpose of this study was to perform chemical analyses of corn oil gavage formulations to determine dose concentrations of m-xylene in preparations used for toxicological testing in rats.

2. MATERIAL:

The m-xylene used in this study, Lot #259211, Batch 286, was obtained from Fluka Chemical Corporation, Hauppauge, New York. It was received March 6, 1986 and assigned LH No. 10,031A. The manufacturer's stated purity was 99%.

3. METHOD AND PROCEDURES

A. Method

The method for the determination of m-xylene in corn oil gavage preparations was developed by Hazleton Biotechnologies Company. In brief, m-xylene is extracted from the corn oil by shaking with methanol. Following centrifugation, appropriate dilutions are made of the extracts, incorporating n-propylbenzene as the internal standard. The extracts are analyzed by gas chromatography (GC) using a flame ionization detector. Matrix standard solutions carried through the procedure are used for the standard curve and instrument calibration. The complete method is included in this report in Attachment A.

Analysis of corn oil for peroxides was performed using the Official Method Cd. 8-53 of the A.O.C.S. (1972). It determines all substances, in terms of milliequivalents (meq) of peroxide per 1000 grams of sample, which oxidize aqueous iodide under the conditions of the test.



METHOD AND PROCEDURES (Continued)

B. <u>Procedures</u>

The chemical characterization of the test material was performed prior to the study start. Identity was determined using infrared (IR), nuclear magnetic resonance (NMR) and mass spectrometry (MS) spectral techniques. Elemental analysis and the determination of water using the Karl Fischer technique were also carried out. A gas chromatographic (GC) scan was run to assess the purity of the chemical.

Upon receipt of the test material, aliquots were taken and stored at -20°C for use as reference standards for subsequent reanalysis. At the end of the study, GC scans for purity were performed on the bulk chemical and the reference standard to assess the integrity of the test chemical under the storage conditions during the study.

The initial method validation for dose verification analysis was performed on matrix standards at 4 levels of concentration (excluding 0). Four standards were prepared at the high and low levels and a single standard at each midpoint. Linear regression analysis was carried out on the results of the standard curve.

In addition, analyses of gavage preparations at the high and low levels of concentration were carried out on two different days to show linearity, precision, accuracy, and reproducibility of the method.

Stability of m-xylene in the corn oil gavage preparations at the high and low dosage concentrations was determined after 7, 14, and 21 days of storage at room temperature and at 5° C.

Dose verification analyses of the corn oil gavage formulations were performed at Weeks 1, 5, 9, and 13 of the study.

Each batch of corn oil used for the preparation of gavage dosing formulations was analyzed for peroxides prior to its first use and at monthly intervals thereafter.

4. RESULTS AND CONCLUSIONS

The purity and identity data for the chemical characterization of the test material are presented in this report as Attachment B.

Tables 1 and 2 contain the analytical method validation data for the determination of m-xylene in corn oil gavage formulations. The RSDs for the four analyses at the high and low points on the standard curve, \pm 0.25% and



4. RESULTS AND CONCLUSION (Continued)

 \pm 0.96, respectively, show excellent precision. The correlation coefficients presented in both tables demonstrate linearity within the range of 0.20 to 1.0 ug m-xylene injected.

Analyses of the gavage samples at the high and low dose concentrations on different days show good method reproducibility and accuracy.

Stability data for m-xylene in corn oil gavage formulations at 40.40 and 323.2 mg/mL concentrations stored at 5°C and room temperature are presented in Tables 3 and 4. After 21 days there was a mean percent loss of 2.8 for samples stored at 5°C and 1.7 for those stored at room temperature. These data clearly indicate the required stability of m-xylene in corn oil for this study.

Results of the dose verification analyses of the gavage preparations for m-xylene can be found in Table 5. All of the samples analyzed were within the acceptable \pm 10% of target concentration. Eight samples had \leq 1.0% agreement between duplicate analyses. The duplicate analyses of 3 samples agreed within 2.5% and the duplicates of one sample varied by 4.3%.

Table 6 presents a summary of the analyses performed to determine peroxides in corn oil. For this study, corn oil with a peroxide number equal to or greater than 10 meq/kg was considered rancid and not acceptable for use. The peroxide number for each analysis was well below the acceptable limit. Copies of the individual reports are included to provide detailed information about the corn oil used and the cumulative results of testing.

Reported by:	
Lee Hohing Research Associate	Date
Approved by:	

Susan A. Lewis, Ph.D. Staff Scientist



TABLE 1

ANALYTICAL METHOD VALIDATION DATA FOR M-XYLENE MATRIX STANDARD PREPARATIONS

M-XYLENE INJECTED (ug)	M-XYLENE FOUND (FROM THE CALIBRATION STANDARD CURVE) (ug)
1.00	$0.999 \overline{x} = 0.999$ $1.002 SD = + 0.0025$ $0.996 RSD = + 0.25\%$ 1.000
0.80 0.40	0.800 0.403
0.20	$0.199 \overline{x} = 0.198$ 0.195 SD = + 0.0019 0.198 RSD = + 0.96% 0.199

Linear Regression Analysis Using Area Ratio:

Correlation coefficient: 1.0000 Intercept: 0.0003 Slope: 0.8989



TABLE 2

ANALYTICAL METHOD VALIDATION DATA FOR THE DETERMINATION

OF M-XYLENE IN CORN OIL GAVAGE PREPARATIONS

SAMPLE IDENTIFICATION	TARGET VALUE (mg/mL)	DATE ANALYZED	ASSAY VALUE (mg/mL)	PERCENT OF TARGET	
Control	0.00	4/03/86	N.D.	N/A	
R0-0277-86A	40.40	4/03/86	38.80	96.04	
R0-0277-86B	40.40	4/03/86	39.20	97.03	
R0-0278-86A	323.2	4/03/86	315.0	97.46	
R0-0278-86B	323.2	4/03/86	313.5	97.00	
Control	0.00	4/04/86	N.D.	N/A	
R0-0277-86A	40.40	4/04/86	38.90	96.29	
R0-0277-86B	40.40	4/04/86	38.65	95.67	
R0-0278-86A	323.2	4/04/86	310.5	96.07	
R0-0278-86B	323.2	4/04/86	310.5	96.07	

STANDARD CURVE STATISTICAL ANALYSIS

Date of Analysis (date extracted):	4/03/86	4/04/86
Correlation Coefficient :	0.9999	1.0000
Intercept :	0.0013	(-)0.0009
Slope :	0.8968	0.9057

N.D. ⇒ None Detected N/A = Not Applicable



TARLE 3

STABILITY OF M-XYLENE IN CORN OIL GAVAGE FORMULATIONS STORED AT 5°C

SAMPLE IDENTIFICATION	DATE FORMULATED	DATE ANALYZED	STORAGE PERIOD	TARGET VALUE (mg/mL)	ASSAY VALUE (mg/mL)	PERCENT OF ORIGINAL X VALUE
R0-0277-86A R0-0277-86B	4/03/86	4/03/86	None	40.40 40.40 x	38.80 39.20 = 39.00	N/A N/A
R0-0278-86A R0-0278-86B	4/03/86	4/03/86	None	323.2 323.2 x =	315.0 313.5 314.3	N/A N/A
R0-0277-86A R0-0277-86B	4/03/86	4/10/86	7 Days	40.40 40.40	39.75 39.55	102 101
R0-0278-86A R0-0278-86B	4/03/86	4/10/86	7 Days	323.2 323.2	324.5 324.0	103 103
R0-0277-86A R0-0277-86B	4/03/86	4/17/86	14 Days	40.40 40.40	39.20 39.15	101 100
R0-0278-86A R0-0278-86B	4/03/86	4/17/86	14 Days	323.2 323.2	312.5 312.0	99.4 99.3
R0-0277-86A R0-0277-86B	4/03/86	4/24/86	21 Days	40.40 40.40	39.30 39.30	101 101
R0-0278-86A R0-0278-86B	4/03/86	4/24/86	21 Days	323.2 323.2	302 309	96.1 98.3

N/A = Not Applicable

L:50/3-3



TABLE 4

STABILITY OF M-XYLENE IN CORN OIL GAVAGE FORMULATIONS STORED AT ROOM TEMPERATURE

SAMPLE IDENTIFICATION	DATE FORMULATED	DATE ANALYZED	STORAGE PERIOD	TARGET VALUE (mg/mL)	ASSAY VALUE (mg/mL)	PERCENT OF ORIGINAL X VALUE
R0-0277-86A R0-0277-86B	4/03/86	4/03/86	None	40.40 40.40 x	38.80 39.20 = 39.00	N/A N/A
R0-0278-86A R0-0278-86B	4/03/86	4/03/86	None	323.2 323.2 x =	315.0 313.5 314.3	N/A N/A
R0-0277-86A R0-0277-86B	4/03/86	4/10/86	7 Days	40.40 40.40	39.60 39.50	102 101
R0-0278-86A R0-0278-86B	4/03/86	4/10/86	7 Days	323.2 323.2	318.0 317.0	101 101
R0-0277-86A R0-0277-86B	4/03/86	4/17/86	14 Days	40.40 40.40	39.30 39.35	101 101
R0-0278-86A R0-0278-86B	4/03/86	4/17/86	14 Nays	323.2 323.2	314.0 312.5	99.9 99.4
R0-0277-86A R0-0277-86B	4/03/86	4/24/86	21 Days	40.40 40.40	39.40 39.40	101 - 101
R0-0278-86A R0-0278-86B	4/03/86	4/24/86	21 Nays	323.2 323.2	309.0 309.0	98.3 98.3

N/A = Not Applicable



TABLE 5

DETERMINATION OF M-XYLENE IN CORN OIL GAVAGE PREPARATIONS TO VERIFY DOSAGE CONCENTRATION

SAMPLE IDENTIFICATION	DATE FORMULATED	DATE ANALYZED	INTERVAL	TARGET VALUE (mg/mL)	ASSAY VALUE (mg/mL)	PERCENT OF TARGET
R0-0295-86	4-09-86	4-09-86	Week 1	0.00	N.D.	N/A
R0-0296-86A	4-09-86	4-09-86	11	40.40	38.70	95.79
R0-0296-86B	4-09-86	4-09-86	11	40.40	38.90	96.29
R0-0297-86A	4-09-86	4-09-86	11	80.80	78.90	97.65
R0-0297-86B	4-09-86	4-09-86	5\$	80.80	78.50	97.15
RO-0298-86A	4-09-86	4-09-86	10	323.2	323.5	100.00
R0-0298-86B	4-09-86	4-09-86	14	323.2	322.5	99.78
R0-0404-86	5-07-86	5-12-86	Week 5	0.00	N.D.	N/A
RO-0405-86A	5-07-86	5-12-86	14	40.40	39.10	96.78
R0-0405-86B	5-07-86	5-12-86	11	40.40	39.10	96.78
R0-0406-86A	5-07-86	5-12-86	19	80.80	78.70	97.40
R0-0406-86B	5-07-86	5-12-86	1)	80.80	78.80	97.52
RO-0407-86A	5-07-86	5-12-86	18	323.2	317.0	98.08
R0-0407-86B	5-07-86	5-12-86	II	323.2	314.5	97.31
R0-0520-86	6-03-86	6-06-86	Week 9	0.00	N.D.	N/A
RO-0521-86A	6-03-86	6-06-86	11	40.40	36.45	90.22
RO-0521-86B	6-03-86	6-06-86	11	40.40	38.20	94.55
RO-0522-86A	6-03-86	6-06-86	11	80.80	78.10	96.66
RO-0522-86B	6-03-86	6-06-86	11	80.80	76.20	94.31
RO-0523-86A	6-03-86	6-06-86	u	323.2	315.0	97.46
R0-0523-86B	6-03-86	6-06-86	11	323.2	307.5	95.14
R0-0708-86	7-01-86	7-03-86	Week 13	0.00	N.D.	N/A
RO-0709-86A	7-01-86	7-03-86	11	40.40	38,95	96.41
R0-0709-86B	7-01-86	7-03-86	II ,	40.40	38.10	94.31
RO-0710-86A	7-01-86	7-03-86	H	80.80	78.10	96.66
RO-0710-86B	7-01-86	7-03-86	10	80.80	78.60	97.28
RO-0711-86A	7-01-86	7-03-86	H	323.2	313.5	97.00
R0-0711-86B	7-01-86	7-03-86	11	323.2	316.5	97.93

N.D. = None Detected N/A = Not Applicable

L:50/5-5



TABLE 6

ANALYSES OF CORN OIL FOR PEROXIDE DETERMINATION

SAMPLE IDENTIFICATION	DATE OF ANALYSIS	PEROXIDE NUMBER FROM EACH INDIVIDUAL TITRATION (meq/kg)
R0-0318-86	04-21-86	$\frac{1.11}{1.07}$ $\frac{1.04}{1.07 + 0.035 \text{ S.D.}}$
RO-0454-86	05-19-86	$\overline{x} = \frac{1.14}{1.14} + 0.006 \text{ S.D.}$
RO-0588-86	06-20-86	$\overline{x} = \frac{1.37}{1.37} + 0.000 \text{ S.D.}$
RO-0810-86	07-17-86	$\frac{1.63}{1.64} = \frac{1.63}{1.63} + 0.006 \text{ S.D.}$



ATTACHMENT A

- Determination of m-Xylene in Corn Oil Gavage (Analytical Method No. 165)
- 2. Analysis of Corn Oil for Peroxides; Modification of the Official Method of the American Oil Chemists' Society



DIAGNOSTIC ASSAYS DEPARTMENT ANALYTICAL CHEMISTRY LABORATORY

ANALYTICAL METHOD NO. 165

PAGE 1 OF 7

DATE: March 24, 1986

APPROVED: Susan A hew-

TITLE: Determination of M-Xylene in Corn Oil Gavage

STRUCTURE:

(CH.

Meta-xylene

DEVELOPED BY: Hazleton Biotechnologies Company, a Division of Hazleton

Laboratories Corporation

1.0 SCOPE

This method is for the gas chromatographic (GC) analysis of m-xylene in corn oil gavage at levels from 40 mg/mL to 320 mg/mL.

2.0 PRINCIPLE

m-Xylene is extracted from the corn oil by shaking with methanol. The extracts are analyzed by gas chromatography (GC) using a flame ionization detector (FID).

PAGE 2 OF 7 DATE: March 24, 1986

3.0 EQUIPMENT

- 3.1 Gas Chromatograph: Hewlett-Packard 5880A equipped with a flame ionization detector (FID), a HP 5880A terminal and a HP 7672A autosampler, or equivalent
- 3.2 Glass Column: 6 ft x 2 mm packed with GP 5% SP-1200/1.75% Bentone 3H on 100/120 Supelcoport, of equivalent
- 3.3 Polypropylene Tubes: Falcon 2070 blue max 50 mL
- 3.4 Analytical Balance: Mettler H31AR, or equivalent
- 3.5 Shaker Box: Equipoise heavy duty, or equivalent
- 3.6 SMI Pipet: 0.1 mL x 0.5 mL SMI pipets, or equivalent
- 3.7 Centrifuge: International centrifuge, model K or equivalent
- 3.8 <u>General Laboratory Glassware</u>

REAGENTS 4.0

- 4.1 Methanol: Baker "HPLC grade", or equivalent
- 4.2 m-Xylene Standard: Fluka Chemical Corp., Cat. No. 95672. Stored at 5°C.
- 4.3 n-Propylbenzene Internal Standard: Supplied by Kodak, Cat. No. 1132224, Lot No. Al3B, stored at 5°C

PAGE 3 OF 7

DATE: March 24, 1986

5.0 PROCEDURE

5.1 Standard Preparation

5.1.1 Preparation of Stock standard solutions

Stock Standard Solution I (10.0 mg/mL): Weigh accurately 500 mg of standard m-xylene (adjust for purity) into a 50 mL volumetric flask. Dissolve and bring to volume with methanol.

Stock Standard Solution II (20.0 mg/mL): Weigh accurately 1000 mg of standard m-xylene (adjust for purity) into a 50 mL volumetric flask. Dissolve and bring to volume with methanol.

5.1.2 Preparation of stock internal standard

Weigh accurately 250 mg of the internal standard n-propylbenzene into a 50 mL volumetric flask. Dissolve and bring to volume with methanol. This internal standard contains 5 mg/mL of propylbenzene.

5.1.3 Preparation of Working Matrix Standard Solutions

Prepare the working matrix standard solutions in 50 mL polypropylene tubes as follows:

Std. Soln.	mL Undosed Corn Oil	mL Stock Std. I	mL Stock Std. II	mL <u>Methanol</u>	Conc. of Extract
1	0.5	1	-	9	1.0
2	0.5	-	1	9	2.0
3	0.5	-	2	8	4.0
4	0.5	5	-	5	5.0

Shake polypropylene tubes on floor shaker for 5 minutes.

Centrifuge at 2500 rpm for 5 minutes.

PAGE 4 OF 7

DATE: March 24, 1986

Dilute extract as follows:

Std. Soln. No.	mL Extract	mL Stock Internal Std.	mL <u>Methanol</u>	Final Concen m-xylene	tration (mg/mL) <u>I STD</u>
1	1	1	8	0.1	0.5
2	1	1-	8	0.2	0.5
3	1	1	· 8	0.4	0.5
4	1	1	8	0.5	0.5

Inject 2 uL of each working matrix standard for standard curve and calibrate.

5.2 Sample Preparation

- 5.2.1 Pipet 0.5 mL of sample into 50 mL polypropylene tubes.
- 5.2.2 Pipet 10 mL methanol into each sample tube.
- 5.2.3 Shake sample tubes on floor shaker for 5 minutes.
- 5.2.4 Centrifuge at 2500 rpm for 5 minutes.
- 5.2.5 Make dilutions of the extracts with methanol in 10 mL volumetric flask as follows:

	mL	mL	Final Conc.	(mg/mL)
<u>Level</u>	Extract	Internal Std.	m-xylene	ISTO
Control	·2	1	0.1	0.5
40 mg/mL	2	1	0.2	0.5
80 mg/mL	1	1	0.4	0.5
320 mg/mL	0.2	1	0.5	0.5

- 5.2.6 Bring to 10 mL volume mark with methanol.
- 5.2.7 Inject 2 uL of sample on GC-FID.
- 5.2.8 Extracts should be refrigerated if not analyzed on the same day.

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DATE: March 24, 1986

5.3 Sample Calculation

- 5.3.1 The Hewlett-Packard GC terminal is programmed to calculate the amount of m-xylene injected from peak area using internal standard procedure for calculating the chromatographic data. The calibration table is generated by analyzing the chromatographic standards listed in 5.1.3.
- 5.3.2

mg detected = $\frac{\text{ug detected}}{\text{mL sample injected}}$

percent target = $\frac{mg \ detected}{target} \times .100$

where mL sample inj. = inj. vol. $x = \frac{mL \text{ sample}}{extraction \text{ volume}} \times \frac{aliquot \text{ taken for dil.}}{final dil. \text{ vol.}}$

PAGE 6 OF 7

DATE: March 24, 1986

7.0 INSTRUMENT PARAMETERS

Gas Chromatograph

: Hewlett-Packard 5880A with flame ionization detector, a HP 5880A terminal, and a HP 7672A

autosampler, or equivalent

Column

: 6 ft x 2 mm glass column packed with GP 5%

SP-1200/1.75% Bentone 34 on 100/120 Supelcoport,

or equivalent

Gas Flow

Carrier Gas Detector Gas : Helium, ~ 30 mL/min : Air, ~ 60 mL/min

Hydrogen, ~ 30 mL/min

Temperature

Oven

75°C

Detector

: 280°C

Injection Port

: 150°C

Injection Volume

: 2 uL

Chart Speed

: 0.25 cm/min

Quantitation

: Peak Area Ratio

Retention Time

: Approx. 4.9 minutes for m-xylene; 8 minutes

for ISTD

NOTE: The above conditions may be changed to optimize the instrument

response and sample detection.

<u>PAGE</u> 7 OF 7

DATE: March 24, 1986

8.0 LIST OF FIGURES

Figure 1. Typical chromatograms, standards

Figure 2. Typical standard curve

Figure 3. Typical chromatograms, samples

```
FIG 1 : TYPICAL CHROMATOGRAMS, STANDARDS
 LIST ATTN 24
 ATTN = 215
 LIST AUTO SEQ 1
 LIST INJ 1 TEMP
 INU 1 TEMP=150°C SETPT=150°C LIMIT=405°C
 LIST DET 1 TEMP
 DET 1 TEMP=280°C SETPT=280°C LIMIT=405°C
 LIST OVEN TEMP ..
OVEN TEMP=75°C SETPT=75°C LIMIT=405°C
EDIT AUTO SEG 6, 1
 EDIT AUTO SEQ 7. 1
START AUTO SED
                                       They I have at working Franchisch
                                                                     9,42
                         mark to the
                                 non-market are interest after and
                          8.22
        /RT: STOP RUN
COPI 5880A SAMPLER INJECTION @ 17:43 APR 17. 1986
  SAMPLE # : ID CODE :
METHOD ABORTED
AREA %
              AREA TYPE, WIDTH HEIGHT BASELINE AREA %
  ₹₹
  ð.90
                            -BASELINE @ START RUN = 8.02
  ଡ଼ି. ଦିମ
                             THRESHOLD @ START RUN = 4
  ଡି. ଫିଡି
                            PEAK WIDTH @ START RUN = 0.08
           9:3859.00 BV
                            0.07 207103.00
0.292 35.94
0.427 136.33
  0.42
                                                          7.94
                                                                  99.523
               647.60 288
3720.89 88
  5.10
                                         35.94
136.33
                                                         , 16.76
                                                                   9.971
  8.22
                                                         11.26
                                                                    0.407
TOTAL APEA = 915227.00
MOLTIFLIER = 1
                   IALIB I
IRUIB AREA OR HEIGHT (1=HEIGHT)0 @ /
      - +
               二面 打
                              ÷<u>₹</u>,=
      원.42원 :
      5.399
             : .2
                                             : MHXYLEHE
      8.223 : 1.8
                              : +IBTB
                                            : PROPYLBENZEN
 3 MULTIPLIER = 1 :
-1 REF window = 5% :
 -2 MON-REF WINDOW = 5% :
 +3 UNCAL RF = 0:
 H4 HERDING
990U. 2399H110 DAV 14 STAB AT RTW 5 555
: PROJ. 2399-108 DAY 14 STAB AT AT 8 5020
```

FIG 1 : TYPICAL CHROMATOGRAMS, STANDAR DS

Dut a c 2 mg pt withing fromtout

EDIT AUTO SEG 6, 2

EDIT AUTO SEO 7, 2

5.10

8.23

START AUTO SEQ

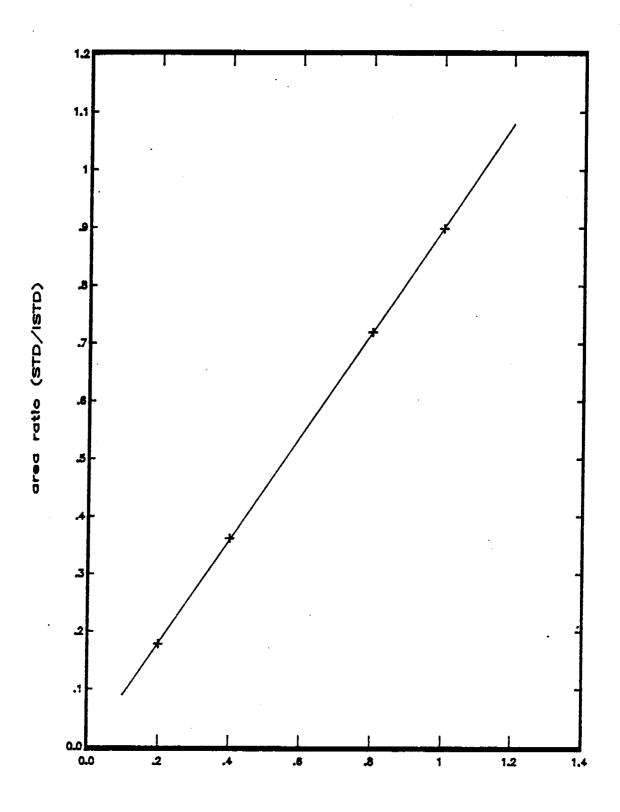
/RT: STOP RUN Kipl 3880A SAMPLER INJECTION @ 17:58 APR 17, 1986 SAMPLE # : ID CODE 2 PROJ. 2399-108 DAY 14 STAB AT RT & 5DEG ISTD 무조 EXP RT AREA TYPE WIDTH CAL AMOUNT NAME 0.00 BASELINE @ START RUN = 7.48 9.00 THRESHOLD @ START RUN = 4 PEAK WIDTH @ START RUN = 0.08 ପି.ପିଡି 5.11 MHXYLENE 5.10 1329.17 BB 0.2861 0.408 8.23 3746.16 + 0.429 2 ISTD 1 8.23 88 PROPYLBENZEN MULTIPLIER = 1 ISTD 1 AMT = 1CACIB 2 CAL RIT NAME AMT 5.105 M-XYLENE : .4 8.234 PROPYLBENZEN 2 : 1.0 EDIT AUTO SEQ 6, 3 EIIT AUTO 8EG 7. 3 START AUTO SEQ to it my me weathing the middle 5.11 √RT: STGP PUN ■103 5880A SAMPLER INJECTION @ 18:14 APR 17, 1986 SAMPLE # : ID CODE PPOU. 2399-108 DAY 14 STAB AT RT & 5DEG 1971 展工 EXP RT AREA TYPE WIDTH CAL AMOUNT NAME ₽.00 BASELINE @ START RUN = 7.12 THRESHOLD & START FUN = 4 ह. हह 0.00 PEAK WIDTH @ START RUN = 0.08 1227 AO 1 2.5 0 00T · 6 - 주주소 : ##도보다 중심소

- 406 -MULTIPLIER = 1 FIG 1: TYPICAL CHROMATOGRAMS, STANDARDS ISTD 1 AMT = 1 CALIB 3 RIT NAME AMT CAL . .8 5.110 M-XYLENE 8.241 PROPYLBENZEN : 1.0 ELIT AUTO SEO 6, 4 EDIT AUTO SEO 7, 4 START AUTO SEQ the constant of the second and and a second 5.11 8.25 FRT: STOP RUN KAPN 5880A SAMPLER INJECTION @ 18:29 APR 17, 1986 SAMPLE # : ID CODE PROJ. 2399-108 DAY 14 STAB AT RT & 5DEG ISTD RT EXP RT AREA TYPE WIDTH CAL AMOUNT NAME ଡ.ଡଡ BASELINE @ START RUN = 7.14 THRESHOLD @ START RUN = 4 0.00 PEAK WIDTH @ START RUN = 0.08 0.00 5.11 5.11 3322.48 BB 0.286 1 1.004 M-XYLENE 9.25 8.25 9.429 PROPYLBENZEN 3702.75 + BB 2 ISTD 1 MULTIPLIER = 1 ISTD : AMT = 1CALIB B 1 CALIB 4 RT NAME OAL 5.112 M-XYLENE 8.247 PROFYLBENZEN : 1.0 EDIT AUTO SEC 6. 5 EDIT AUTO SEG 7, 13

5.12 8.26 RT: STOP RUN

START AUTO SEG

FIGURE 2 - STANDARD CURVE m-xylene



ug m-xylene standard injected

```
AMOUNT NAME
  RT
       EXP RT
                         AREA
                                TYPE WIDTH CAL
                            BASELINE @ START RUN = 7.04
  0.00
                            THRESHOLD @ START RUN = 4
  0.00
                           PEAK WIDTH @ START RUN = 0.08
  0.00
                                                  0.786 M-XYLENE
                                88 0.288
  5.12
         5.12
                      2608.91
                                              1
                                                  ISTD 1 PROPYLBENZEN
                                     0.430
                                              2
         8.26
                      3716.91 + 88
  8.26
MULTIPLIER = 1
                         FIG 3, TYPICAL CHROMATOGRAMS, SAMPLES .
ISTD 1 AMT = 1
                                         Ty. 0277-865
                            5.12
                          8.26
        RT: STOP RUN

₹ 58804 SAMPLER INJECTION @ 18:58 APR 17, 1986

  SAMPLE # : ID CODE
PROJ. 2399-108 DAY 14 STAB AT RT & 5DEG
ISTE
                         AREA TYPE WIDTH CAL AMOUNT NAME
  FT EXP RT
                            BASELINE @ START RUN = 8.10
 0.00
                            THRESHOLD @ START RUN = 4
  0.00
                            PEAK WIDTH @ START RUN = 0.08
 0.00
                                 BB 0.288
                                              1
                                                    0.787 M-XYLENE
  5.12
                      2621.22
         5.12
                                              2
         8.26
                      3728.72 + 88
                                      0.430
                                                  ISTD 1 PROPYLBENZEN
  8.26
MULTIPLIER = 1
ISTD : AMT = 1
                                            RJ - 3277- F. A.
                            5.12
                          8.26
        RT: STOP RUN
# no # 5889A SAMPLER INJECTION @ 19:10 APP 17. 1986
  Samele # : ID CODE
PROL. 2799-108 DAY 14 STAB AT RT & 5DED
1977
  RT ENP RT
                         AREA TYPE WIDTH CAL AMOUNT NAME
                            BASELINE @ START RUN = 8.19
 \theta. \theta
                            THRESHOLD @ START RUN = 4
 គ្.គ្ន
                            PEAK WIDTH @ START RUN = 0.08
  ତି.ଡିଡ
                      2611.95 88 0.287
                                             1
                                                   0.784 M-XYLENE
  5.13
         5.12
                                      0.430
  8,26
                      3729.92 + 88
                                              2
                                                  ISTD 1 PROPYLBENZEN
         8.26
MILTIPLIER = 1
1975 : 467 = 1
```

7. Analysis of Corn Oil for Peroxide

- a. Any batch of corn oil used in the Bioassay Program will be analyzed for peroxides before it is first used and at monthly intervals thereafter, while it is in use. Corn oil must be purchased in batches no smaller than 2 gallons (7 kg) per chemical for which it is the dose vehicle, unless substantially less than this quantity is being used monthly. All corn oil must be stored at 5° C or lower.
- b. The following is a standard analytical procedure which can be used for these analyses. The method employed is the Official Method Cd. 8-53 of the A.O.C.S. (1972).1/ It determines all substances, in terms of milliequivalents (meq) of peroxide per 1,000 grams of sample, which oxidize aqueous iodide under the conditions of the test. These are

This is a contractually specified method.

Notes. 1) Boil and cool all H20.

2) Pregare 0.005 N This elike by dilution
of a commercial standardized this entitle to mount
of greater incrinality

Jeny!!. Petgenil 8/26/51

Official and Tentative Methods of the American Oil Chemists' Society, 3rd Ed. Revised; V.C. Mehlenbacher, T.H. Hopper, E.M. Sallee, and W.E. Link, Eds., American Oil Chemists' Society, Champaign, Illinois (1972).

& 1

generally assumed to be peroxides or other similar products of fat oxidation. The method is highly empirical, and any variation in procedure may affect the results.

A 5.0 gram sample of the corn oil to be analyzed is quantitatively transferred into a 250 ml titration flask and 30 ml of glacial acetic acid:chloroform (60:40 v/v) is added. The mixture is stirred until the corn oil has completely dissolved. One-half milliliter of a saturated aqueous potassium iodide solution is added. The test solution is stirred thoroughly and allowed to stand for exactly I minute, after which 30 ml of distilled water is added. The iodine liberated by the peroxides in this solution is titrated potentiometrically with standard 0.005 N sodium thiosulfate solution, stirring vigorously to ensure thorough mixing. An automatic titrator with platinum disk working electrode and silver - silver chloride reference electrode is convenient. Titrations should be run in triplicate. A blank titration of reagents should be run on the day the oil sample is analyzed; the blank should not titrate more than 1.0 ml of the 0.005 H sodium thiosulfate standard solution. Peroxide number, expressed in milliequivalents of peroxide per kilogram of oil (meq/kg), is calculated as follows:

Peroxide Number = $(\nabla - B) \times R \times 1,000$

- ∇ = volume (in ml) of thiosulfate solution required for titration of oil sample
- B = volume (in ml) of thiosulfate solution required for titration of reagent blank
- m = normality of sodium thiosulfate solution
- W = Weight of oil sample in grams
- Results should be reported as shown in Figure 13 to this Attachment A. In this report, the method above can be cited by reference to this document, but the instrument used for the titration must be specified. When reporting follow-up analyses, the dates and results of all previous analyses of the batch should be included for comparison. Conclusions and actions taken as a result must be noted, and the report must be signed and dated by the reponsible chemist. These reports should accompany the first Monthly Progress Report after the analysis.
- Corn oil with a peroxide number equal to or less greater than 10 meq/kg will be considered rancid for purposes of this program and must be replaced immediately.

Pootnotes:

^{(&}amp;1A) Changed 10/26/79 by Modification 70

Dist. G. Wolfe, I. Foxx, M. Rodwin, Project File

ANALYSIS FOR PEROXIDES IN CORN OIL

Bioassay Lab: Hazleton Biotechnologies Company

Type (brand) of corn oil: Duke's Pure Corn Oil

Source: Mazo Lerch Co.

Lot or batch number (if any): Lot No. 5K21

Additives (if known): Not indicated

Date procured: 1/14/86

Storage temperature: 4°C - Rockville, walk-in refrigerator

Used for: Gavage vehicle

Analytical Method: MRI modification of AOC/AOAC method

Digital MV meter used with a platinum combination electrode (platinum/AG/AgCl), Fisher Cat. No.

13-639-82.

Date of Analysis	Peroxide Number (from each individual titration, meq/kg)	Average Peroxide Number (meq/kg)
4/21/86	1.11, 1.07, 1.04	1.07 ± 0.035 S.D.
Previous Analyses		
1/31/86 3/03/86	0.611, 0.616, 0.611 0.893, 0.888, 0.892	0.613 ± 0.003 S.D. 0.891 ± 0.003 S.D.

Conclusions: Peroxide number is well below the limit of 10 meq/kg.

Signed Lee Hoking Date 5-16-86

Approved

Susan to hours

Dist. G. Wolfe, I. Foxx, M. Rodwin, Project File

ANALYSIS FOR PEROXIDES IN CORN OIL

Bioassay Lab: Hazleton Biotechnologies Company

Type (brand) of corn oil: Schneck's Corn Oil

Source: Mazo Lerch Co.

Lot or batch number (if any): Lot No. 775

Additives (if known): Not indicated

Date procured: 5/15/86

Storage temperature: 4°C - Rockville, walk-in refrigerator

Used for: Gavage vehicle

Analytical method: MRI modification of AOC/AOAC method

Digital MV meter used with a platinum combination electrode (platinum/AG/AgCl), Fisher Cat. No.

13-639-82.

Date of Analysis	Peroxide Number (from each individual titration, meq/kg)	Average Peroxide Number (meg/kg)	
5/19/86	1.14, 1.14, 1.13	1.14 ± 0.006 S.D.	

Previous Analyses

Conclusions: Peroxide number is well below the limit of 10 meg/kg.

Signed lice Hohwing Date 5-20-86

Approved / Junio & Structure

Dist. 1. wolfe, I. Foxx, M. Rodwin, Project File

ANALYSIS FOR PEROXIDES IN CORN OIL

Bioastay Lab: Hazleton Biotechnologies Company

Type (brand) of corn oil: Schneck's Corn Oil

Source: Mazo Lerch Co.

Lot or batch number (if any): Lot No. 775

Additives (if known): Not indicated

Date procured: 6/20/86

Storage temperature: 4°C - Rockville, walk-in refrigerator

Used for: Gavage vehicle

Analytical method: MRI modification of AOC/AOAC method

Digital MV meter used with a platinum combination electrode (platinum/AG/AgCl), Fisher Cat. No.

13-639-82.

Date of Analysis	Peroxide Number (from each individual titration, meq/kg)	Average Peroxide Number (meg/kg)
6/20/86	1.37, 1.37, 1.37	1.37 ± 0.00 S.D.
Previous Analyses		
5/19/86	1.14, 1.14, 1.13	1.14 ≠ 0.00€ S.D.

Conclusions: Peroxide number is well below the limit of 10 meg/kt.

Signed hee Hahing

Approved

Janua Donkun

ANALYSIS FOR PEROXIDES IN CORN OIL

Bioassay Lab: Hazleton Biotechnologies Company

Type (brand) of corn oil: Schneck's Corn Oil

Source: Mazo Lerch Co.

Lot or batch number (if any): Lot No. 775

Additives (if known): Not indicated

Date procured: 6/20/86

Storage temperature: 4°C - Rockville, walk-in refrigerator

Used for: Gavage vehicle

Analytical method: MRI modification of AOC/AOAC method

Digital MV meter used with a platinum combination

electrode (platinum/AG/AgCl), Fisher Cat. No.

13-639-82

Date of Analysis	Peroxide Number (from each individual titration meq/kg)	Average Peroxide Number (meq/kg)
7/17/86	1.63, 1.64, 1.63	1.63 ± 0.006 S.D.
Previous Analyses	•	
5/19 /86 6 /20/86	1.14, 1.14, 1.13 1.37, 1.37, 1.37	1.14 ± 0.006 \$.D. 1.37 ± 0.00 \$.D.

Conclusions: Peroxide number is well below the limit of 10 meq/kg.

Signed LC Date

1-18-86

Approved

Susan A hards



ATTACHMENT B

Chemical Characterization of the Test Material:

- Report of Analysis, Hazleton Laboratories America, Madison, Wisconsin.
 - a Moisture, Karl Fischer method
 - b GC purity
 - c IR spectra
 - d GCMS
 - e NMR
- 2. Elemental analysis, Micro-Tech Laboratories, Inc., Skokie, Illinois.
- 3. Report of Analysis, Hazleton Laboratories America, Madison, Wisconsin.
 - a Final GC purity

1301 KINSMAN BLVD. • P.O. BOX 7545 • MADISON, WISCONSIN 53707 • PHONE (608) 241-4471 • TLX 703956 HAZRAL MDS UD

REPORT OF ANALYSIS

LEE HOHING

HAZLETON BIOTECHNOLOGIES CORPORATION

9200 LEESBURG TURNPIKE

UIENNA, VA 22180

SAMPLE NUMBER: 6030271

DATE ENTERED: 03/13/8c

REPORT PRINTED: 04/30/8c

M-XYLENE (RO-0218 86)

PURCHASE ORDER NUMBER: 002107

ASSAY ANALYSIS UNITS
MOISTURE, KARL FISCHER METHOD .173 %

G.C. PURITY

TURE BY G.C. ANALYSIS

99.1 %

METHOD REFERENCE

HAZLETON LABORATORY WORKSHEET 05XX 000166-00.

IR SPECTRA

EXHIBITS CHARACTERISTIC PEAKS FOR THIS COMPOUND

METHOD REFERENCE

ALDRICH REFERENCE BOOK OF IR SPECTRA.

GOMS

REPORT TO BE GENERATED MANUALLY

NMR

REPORT TO BE GENERATED MANUALLY

 CARBON
 86.51
 %

 HYDROGEN
 9.38
 %

 OXYGEN
 0.35
 %

METHOD REFERENCE

ANALYSIS PERFORMED BY MICRO-TECH LABORATORIES, INC., SKOKIE, IL

3301 KINSMAN BLVD. • P.O. BOX 7545 • MADISON, WISCONSIN 53707 • PHONE (608) 241-4471 • TLX 703956 HAZRAL MDS UD

AMPLE NUMBER: 60302710

PAGE

2

M-XYLENE (RO-0218 86)

METHOD REFERENCES

MOISTURE, KARL FISCHER METHOD UNITED STATES PHARMACOPEIA, VOLUME XX, PAGE 988 (1980).

METHOD LISTED ABOVE WITH RESULTS

GCMS METHOD PER ANALYSIS



THE UNIVERSITY OF WISCONSIN-MILWAUKEE/P.O. Box 413, Milwaukee, Wisconsin 53201

COLLEGE OF LETTERS AND SCIENCE DEPARTMENT OF CHEMISTRY

PHONE: (414) 963-4411

To:

Joe Polywacz

Hazleton Laboratories

From:

James Otvos, Asst. Professor

Re:

NMR analysis of LIMS #'s 60301753-60301754 and

60302709-60302711

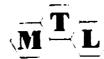
HLA-VA

Date:

April 21, 1986

Enclosed are 1H NMR spectra of p-xylene(60302709), m-xylene(60302710), and o-xylene(60301754) in deuterochloroform solvent which positively confirm their identities. The o-xylene sample was labeled "o-xylol", but is in fact xylene. An unexpected peak at 2.21 ppm was found in the p-xylene sample which was attributed to a solvent contaminant (probably H2O) since a 13C NMR spectrum of the same sample failed to exhibit any extra resonances. The three xylene samples are at least 98% pure as judged by the intensities of several small resonances of unknown origin in the spectra.

13C spectra were taken of the remaining two samples, strychnine (60301753) and brucine (60302711), because they are much more diagnostic of the structures of these compounds compared to ¹H spectra. As the enclosed spectra indicate, the samples are pure. The number of resonances observed in each spectrum and their chemical shifts confirm the identities of the two compounds.



MICRO-TECH LABORATORIES, INC.

4117 OAKTON STREET SKOKIE, ILLINOIS 60076

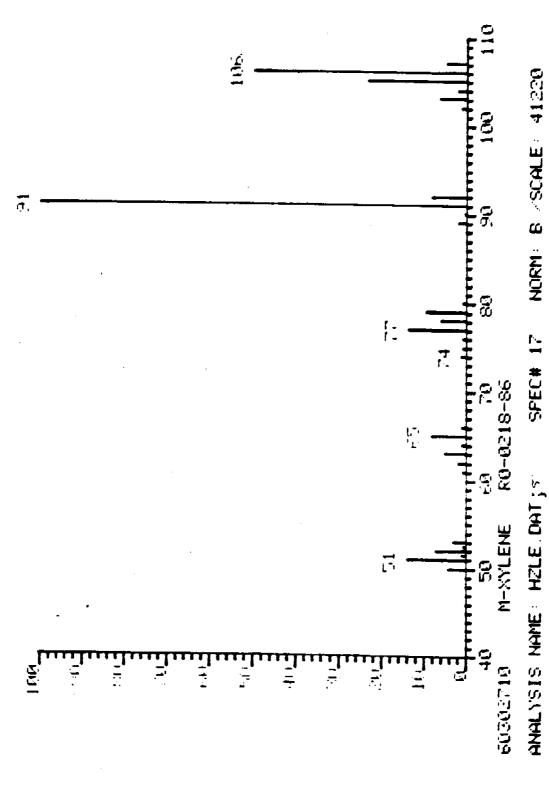
April 10, 1986

Mr. L. Evarts
Hazleton Laboratories America, Inc.
3301 Kinsman Boulevard
P.O. Box 7545
Madison, Wisconsin 53704

SAMPLE NO	%C	%H	%N	C1%	s %	0 %
60302709	88.05	9.36				0.26
50302710	86.51	9.38				0.35
60302711	59.19	6.21	6.15	0.49	3.63	19.52
				F	ECEIV	ED.
			•		DD 111	
				HI	A Mad	aosir

Very truly yours,

June B. Gast



Not DATE: APR 2 86 13:16:51

Amery 2 3 1/86

35%: S APR 2 86	LIST OF	HH00:[00 16:34	7,3001HZL VERSION		60302710 Page: 1	m-xylene	Ro-0318-86 .
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3	51.6	376.	0.91				
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5	52.1	360.	0.87				
ర	52.6	240.	0.58				
7	53.1	1216.	2.95				
ខ	61.1	276.	0.67				
ပ္	62.1	788.	1.91				
1 ()	63.1	2108.	5.11				
1.1	64.1	408.	0.99				•
1.2	65.1	3404.	8.26				
13	66.1	396.	0.96				•
1.4	74.1	443.	1.09				
15	75.0	448. 296.	0.72		•		
1 4	76.1	336.	0.82				
17	77.1	5604.	13.60				
. 18	78.1	2448.	5.94				
19	79+1	3912.	9.49				
20	80.1	288.	0.70				
21	89.1	772.	1.87				
22	90.1	152:	0.37				
23	91.1	41220.	100.00				
24	92.1	3356.	8.14				
25	102.1	484.	1.17			•	
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27	103+2	364.	0.88			•	•
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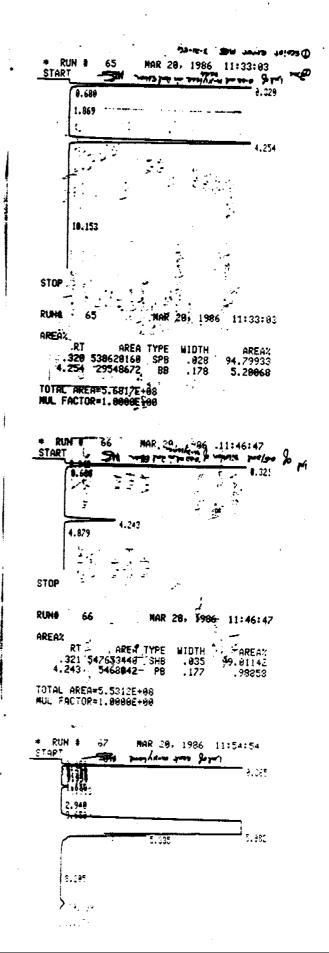
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3301 KINSMAN BLVD. • P.O. BOX 7545 • MADISON, WISCONSIN 53707 • PHONE (608) 241-4471 • TLX 703956 HAZRAL MDS UD

REPORT OF ANALYSIS

LEE HOHING HAZLETON BIOTECHNOLOGIES CORPORATION 9200 LEESBURG TURNPIKE VIENNA, VA 22180

SAMPLE NUMBER: 6070623

DATE ENTERED: 07/30/8

REPORT PRINTED: 10/29/8

M-XYLENE: RO-0311-86

REFERENCE CHEMICAL

FINAL PURITY

PURCHASE ORDER NUMBER: 0A12550

SEE ATTACHED CHROMATOGRAMS

METHOD_REFERENCES

METHOD LISTED ABOVE WITH RESULTS

3301 KINSMAN BLVD. • P.O. BOX 7545 • MADISON, WISCONSIN 53707 • PHONE (608) 241-4471 • TLX 703956 HAZRAL MDS UD

REPORT OF ANALYSIS

LEE HOHING

HAZLETON BIOTECHNOLOGIES CORPORATION

9200 LEESBURG TURNPIKE

VIENNA, VA 22180

SAMPLE NUMBER: 6070623

DATE ENTERED: 07/30/8

REPORT PRINTED: 10/29/8

M-XYLENE: RO-0926-86

BULL CHEMICAL

FINAL PURITY

PURCHASE ORDER NUMBER: 0A12550

SEE ATTACHED CHROMATOGRAMS

METHOD_REFERENCES

METHOD LISTED ABOVE WITH RESULTS

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- 431 -

APPENDIX 10

Study Protocol and Amendments

- 432 -



1330 - 8 PICCARD ORIVE. ROCKVILLE MARYLAND ROSSO

PROJECT NO. 2399-108 DATE	ISSUED April 7, 1986
PROPOSAL NO. 5-580 STUDY TITLE:	Subchronic Toxicity in Rats
TEST MATERIAL (s): Safety, storage, and descriptive	information is attached.
A. Identification m-Xylol (m-Xylene)	
B. Lot No. (s) 259211 286	
C. Receipt Date March 6, 1986	
D. LH Number (s) 10,031A	
STUDY LOCATION: Rockville	PROPOSED INITIATION DATE: April 11, 1986 PROPOSED COMPLETION OF IN-LIFE PHASE DATE: July 10, 1986
DISTRIBUTION: ORIGINAL SIGNED PROTOCO	L TO PSO
FIXED DISTRIBUTION: (No. Copies)*	PERFORMING DEPARTMENTS (4) CONTROL (4) CON
Health Services (1) Compound Prep (Tox) (1) Scientific Res. (Tox) (2) (1) Cuality Assurance (1) Contracts (1) Client Services (1)	Toxicology (2) Analytical Chemistry (1
Lab Animal Medicine (1) Sponsor (1)	Pathology (4)
* Unless otherwise directed.	•
Protocol is Attached.	
Date and Means of Sponsor Authorization:	•
Signed protocols to be forwarded by	sponsor.
This protocol issued to permit sche	duling of the study by the laboratory.
,	· .
	•
•	Lang W. Wolfe
STUD	Y DIRECTOR: Gary W. Wolfe, Ph.D., D.A.B.T.
	DATE: 4/9/86

Form No. 5 Revised 8-85



PROTOCOL

Project No. 2399-108

1. Study

Subchronic Toxicity Study in Rats

2. Purpose

To evaluate the subchronic toxicity of a test material when administered daily via oral gavage to rats for 90 days.

3. Study Location

Hazleton Laboratories America, Inc. 1330-B Piccard Drive

Rockville, Maryland 20850

4. Sponsor and Address

Dynamac Corporation 11140 Rockville Pike

Rockville, Maryland 20852

5. HLA Study Director

Gary W. Wolfe, Ph.D., D.A.B.T.

6. HLA Study Coordinator

Marcia P. Rodwin, B.A.

Regulatory Compliance

This study is subject to applicable regulations of the Environmental Protection Agency and will be conducted per EPA Pesticide Assessment Guidelines, Subdivision F, Section 158.82-1, Toxic Substances Control Act (TSCA) Testing Guidelines for Ninety Day Subchronic Toxicity Studies, 40 CFR 798.2650, and in accordance with the Good Laboratory Practice Standards, 40 CFR Part 160.

8. Quality Assurance

The protocol, in-life phase, interim report and the final report will be audited by Quality Assurance in accordance with standard operating procedures at Hazleton Laboratories.

9. Proposed Study Timetable

Initiation: -April 11, 1986

Terminal Sacrifice: July 10, 1986

Final Report: September 5, 1986



- 2 -

Project No. 2399-108

10. Test Material

A. Identification

m-Xylene (CAS 108-38-3)

B. Purity

99%

C. Characteristics

Purity and identity will be determined prior to study initiation, and purity only at termination. (If identity has been established for a 14-day study then only purity needs to be determined prior to start of 90-day study.)

D. Reserve Samples

Reserve samples (4 x 10 g) of the test and control articles will be taken at initiation and retained frozen. These archived samples of the test article will serve as reference standards for subsequent purity analyses. These samples, as well as any remaining test material, will be discarded upon acceptance of the study results for regulatory purposes (May 8, 1987).

11. Experimental Design

A. Animals

(1) Species

Rat

(2) Strain/Source

Sprague-Dawley/Charles River

(3) Age at Initiation

Preferably before 6 weeks of age, but not more than 8 weeks of age.

(4) Number/Sex

80/sex

(5) Identification

Individual eartags

(6) Husbandry

(a) Housing

Individual



.- 3 -

Project No. 2399-108

(b) Food

Purina Certified Rodent Chow 5002, ad libitum. Feed is analyzed by the manufacturer for concentrations of specified heavy metals, aflatoxin, chlorinated hydrocarbons, organophosphates, and specified nutrients. (See Attachment #1 for details).

(c) Water

Acidified water, ad libitum. Water is analyzed twice per year for contaminants as listed in the EPA drinking water standards.

(d) Contaminants

The study director and/or the sponsor have considered possible interfering substances potentially present in animal feed and water, including the test material itself or possible structurally related materials as well as the items listed in (b) and (c) above. None of these contaminants are reasonably expected to be present in animal feed or water at levels sufficient to interfere with this study.

(e) Environment

Every attempt will be made to maintain temperatures at $69 - 78^{\circ}F$ with a relative humidity of $50 \pm 20\%$. A 12-hour light/12-hour dark cycle will be maintained. Temperature and humidity will be recorded twice daily.

(f) Quarantine

Approximately two weeks. Animals selected for study will have been determined to be acceptable for admission to the study.

(7) Randomization

Using computer-generated random numbers with assignment to groups. At the time of randomization, the weight variation of the animals of each sex used should not exceed ±2 S.D. of the mean weight, and the mean body weights for each group of each sex will not be statistically different.



. 4 -

Project No. 2399-108

(8) Justification

Sprague-Dawley rats historically have been used in safety evaluation studies and are requested by EPA.

B. Group Designation and Dosage Levels

Group No.	No. of	Animals	Dosage Levels
	Male	Female	mg/kg/day
1 (Control)	20	20	0
2 (Low)	20	20	100
3 (Mid)	20	20	ಎ ാ0
4 (High)	20	20	800

- C. Dosing Procedures
 - (1) Method of Oral gavage, 7 days per week for 13 weeks.
 Administration Treatment will continue until the day before necropsy.
 - (2) Reason for Dosing Route

Potential human exposure is by the oral route.

(3) Preparation of Dosing Formulations

Fresh dosing formulations will be prepared based on stability study. Dosing formulations will be prepared using corn oil and adjusted to 100% compound activity. Dosing factor will be 2.5 ml/kg. Reserve samples from each mixed batch will be retained for possible analysis. These samples will be discarded upon acceptance of the final report.

- (4) Analysis of Dosing Formulations
 - (a) Stability

Samples of the lowest level will be analyzed at Day 0 and after 7, 14, and 21 days under conditions of use and under refrigeration.

(b) Homogeneity

If the dosage formulation is a suspension, homogeneity of each formulation will be confirmed by analyzing the top, middle, and bottom of each formulation prior to study initiation. If the dosage formulation is a single phase, no homogeneity is required.



- 5 -

Project No. 2399-108

(c) Routine Analyses

Each dosage formulation for weeks 1, 5, 9, and 13 will be analyzed for test material.

(5) Absorption

Though the purpose of this study is not to determine absorption of the test material, toxic or pathologic effects will serve as evidence of absorption.

- D. Observation of Animals
 - (1) Clinical Observations

Twice daily - mortality and morbidity check.

Once daily - cageside observation for obvious indications of a toxic effect, will be recorded about one hour after completion of dosing. In addition, a cursory exam will be conducted while dosing.

Data for specific observations will be recorded on separate forms. Because these are cageside animal checks, the observations will not be as specific as and may not necessarily duplicate those observations recorded on body weight days when thorough physical examinations are conducted.

(2) Physical Examinations

At each weighing interval.

(3) Body Weights

Prior to treatment, at initiation and weekly thereafter.

(4) Food Consumption

Weekly

(5) Ophthalmoscopic Examinations

Prior to treatment and during week 13 using indirect ophthalmoscopy on the last ten animals per sex per group.

- E. Clinical Pathology
 - (1) Frequency

Prior to initiation and during weeks 4 and 13.



- 6 -

Project No. 2399-108

Blood will be collected via orbital sinus with ${\rm CO_2}$ anesthetization.

(2) Number of Animals

'(a) Prior to initiation

5/sex randomly selected from animals acceptable for study but not used on study.

(b) During Weeks 4 and 13

10/sex/group (sampled per SOP)

(3) Tests

(a) Hematology

leukocyte count
erythrocyte count
hemoglobin
hematocrit
platelet count
differential leukocyte count
reticulocyte count

(b) Blood Chemistry

sodium potassium chloride total protein albumin calcium phosphorus total bilirubin urea nitrogen creatinine glucose SGOT/AST SGPT/ALT globulin alkaline phosphatase cholesterol albumin/globulin ratio LDH



- 7 -

Project No. 2399-108

F. Termination

(1) Unscheduled Sacrifices and Deaths

Necropsies, by trained personnel using procedures approved by board-certified pathologists, will be conducted on all moribund animals and on all animals that die.

(2) Terminal Kill

After 13 weeks of treatment, all surviving animals will be weighed, killed by $\rm CO_2$ intoxication and subjected to a complete gross necropsy. Necropsies will be conducted by trained personnel under the direct supervision of a board-certified pathologist.

G. Postmortem Procedures

(1) Gross Necropsy

The necropsy will include examination of:

The external surface All orifices Cranial cavity Carcass

External surface of the brain (at necropsy). Cut surfaces of the brain and spinal cord will be examined at the time of tissue trimming.

The thoracic, abdominal and pelvic cavities and their viscera

The tissues and organs of the neck region

Findings will be recorded.

(2) Organ Weights

For each terminally killed animal, the following organs will be weighed following careful dissection and trimming to remove fat and other contiguous tissue in a uniform manner:

liver kidneys spleen

adrenals testes/ovaries

brain heart



- 8 -

Project No. 2399-108

(3) Tissue Preservation

The following tissues from each animal will be preserved in 10% neutral buffered formalin:

all gross lesions kidneys skin brain with brainstem adrenals epididymis (medulla/pons, cerepancreas prostate bellar cortex, and testes seminal vesicles cerebral cortex) ovaries pituitary uterus thyroid with parathyroids spleen thymus aorta lungs esophagus trachea stomach (forestomach and glandular) heart duodenum, jejunum, ileum salivary glands colon, cecum, rectum (mandibular) urinary bladder liver mesenteric lymph node sternum with bone marrow sciatic nerve mammary gland femur including articular surface thigh musculature cervical spinal cord eyes mid-thoracic spinal cord lumbar spinal cord exorbital lacrimal glands

Electron microscopy will be conducted on livers from control, 200, and 800 mg/kg groups. Detailed methodology will be issued as an amendment to the protocol.

(4) Histopathology

All preserved tissues from all animals will be embedded in paraffin, sectioned, and stained with hematoxylin and eosin.

The following tissues will be examined microscopically:

- (1) All tissues from control and high-dose animals and from all animals not surviving to termination.
- (2) Gross lesions, lungs, liver, and kidneys from all remaining animals.
- (3) Target organs noted at the high-dose level from all animals.



- 9 -

Project No. 2399-108

12. Reports

Following termination of the study, a report which includes the following information (as appropriate) will be prepared and submitted:

- Experimental Design and Methods
- Results:

mortality
clinical observations
body weights and
food consumption
clinical pathology tests

ophthalmoscopic findings organ weights and organ/body weight ratios gross pathology histopathology

- Statistical Analyses:

Statistical methods will be those presented in Attachment #2.

- Statistical Evaluation:

survival rates growth rates and/or absolute body weights total food consumption clinical pathology values
organ weights and organ/
body weight ratios

- Tables:

mean food consumption values
cumulative survival rates and
mean body weights
summary of clinical
signs for each test group
to include: a list of each
finding and number of
animals affected

summary incidence of ophthalmoscopic findings mean clinical pathology values mean organ weights and organ/body weight ratios summary incidence of gross pathology findings summary incidence of histopathology findings



- 10 -

Project No. 2399-108

- Appendices

week of death for each animal individual body weights individual food consumption individual clinical signs for each animal to include: the week of observation of each sign, a description of each sign, and its subsequent course individual clinical pathology values

individual ophthalmoscopic
 findings
individual organ weights and
 organ/body weight ratios
individual gross pathology
 findings
individual histopathology
 findings
analytical chemistry methods and
 results

The final report, or a draft copy of such, will be reviewed by the sponsor within 1 month after receipt. Any revisions or comments will be submitted to Hazleton within this period.

13. Record Retention

All tissue specimens, blocks and slides, and copies of all raw data and the final report will be retained by Hazleton Laboratories. Tissue specimens will be discarded as per work assignment.



- 11 -

Project No. 2399-108

SIGNATURE PAGE

Hazleton Laboratories America, Inc.:

Sponsor:

May W. W. W. Study Director, Toxicology

Date: 3/14/86

1-23-86

· - 2/24/85

Date:

APPROVED BY:



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Project No. 2399-108

ATTACHMENT #1

CONTAMINANT ANALYSIS FOR CERTIFIED RODENT CHOW 5002 AND WATER

This information identifies the potential contaminants monitored for both laboratory feed and water. The Certified Rodent Chow data are provided by the manufacturer.

Certified Rodent Chow[®] 5002 certification profile:

	Maximum
<u>Heavy Metals</u>	Concentration
Arsenic	1.0 ppm
Cadmium	.5 ppm
Lead	1.5 ppm
Mercury	.2 ppm
<u>Aflatoxin</u>	10 ppb
Chlorinated Hydrocarbons and PCB	
Aldrin	.05 ppm
Dieldrin	.05 ppm
Endrin	.05 ppm
Heptachlor	.05 ppm
Heptachlor Epoxide	.05 ppm
Lindane	.05 ppm
Chlordane	.05 ppm
DDT-Related Substances	.15 ppm
PCB	.15 ppm
Organophosphates	
Thimet	.5 ppm
Diazinon	.5 ppm
Disulfaton	.5 ppm
Methyl Parathion	.5 ppm
Malathion	.5 ppm
Parathion	.5 ppm
Thiodan Ethion	.5 ppm-
Trithion	.5 ppm .5 ppm
TT TOTAL	.5 ppm



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ATTACHMENT #1 (Continued)

2. Standard contaminant analysis for water includes:

Barium
Cadmium
Chromium
Copper
Fluorine
Iron
Lead
Manganese
Mercury
Selenium
Sodium
Sulfate
Ammonia
Total Nitrogen
Chloride

DDE, DDD, DDT
PCB
Dieldrin
BHC
Lindane
HCB
Endrin
Heptachlor Epoxide
2,4-D
Silvex (2,4,5-TP)
Color Test
Turbidity
Arsenic
Silver
Zinc



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ATTACHMENT #2

Analysis of Data

If appropriate, cumulative survival will be analyzed using the National Cancer Institute Package. Trend analysis of survival will be evaluated at the 5.0% one-tailed probability level. Control vs. test group comparisons of survival will be evaluated at the 5.0% one-tailed probability level if trend analysis is significant or at the 5.0% two-tailed probability level if trend analysis is not significant.

Growth rates and other data will be analyzed in the order presented in the flowchart. Tests for homogeneity of variances, ANOVA and the Terpstra-Jonckheere Nonparametric Test for Trend will be evaluated at the 5.0% one-tailed probability level.



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ATTACHMENT #3

Protocol Addendum

ANALYTICAL CHEMISTRY

Introduction

The purpose of this work is to provide chemical support for the bioassay studies. This support consists of purity, identity and stability of the bulk compound and development of a method to determine the concentration stability and homogeneity (when indicated) in the dosing vehicle. If the dosing vehicle is corn oil, determination of peroxides in the corn oil will be carried out.

Chemical Characterization of Test Article

The physical appearance will be noted and the source of the chemical together with the manufacturer's stated purity will be reported. The following spectral techniques will be employed initially: Infrared (IR), nuclear magnetic resonance (NMR) and mass spectrometry (MS). Spectra obtained will be compared to literature references¹ and consistency to expected structure. Elemental analysis and determination of water using the Karl Fischer technique will be carried out. A gas chromatographic (GC) technique will be used to assess purity and compared, whenever possible, to known reference standards, if available. Reference samples will be taken on receipt of chemicals and stored frozen for future reanalysis. The GC scan for purity will be carried out and compared to the reserve sample after 4 months (or on receipt of chemical, at the end of the 14-day study and at the end of the 90-day study if more than 4 months have elapsed). Thus, the integrity of and purity of the test article throughout the study will be documented. It is important to choose a GC column that will effectively separate the o-, m- & p-isomers (see Methodology).

Determination of the Test Article in the Dosing Vehicle

Method Validation

A four-point standard curve will be used (excluding 0). Matrix standards and/or spike recoveries will be used if applicable. Imprecision of the low and high standard will be reported as percent relative standard deviation (% RSD) (n=4) and the middle standards will be analyzed twice. The % RSD should be less than 5%. Linear regression analysis will be carried out of the results of the standard curve.

¹Sadtler Standard Spectra, Philadelphia, PA.



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ATTACHMENT #3 (Continued)

Prior to the study start, compound preparation will mix the low and the high dosage groups. These samples will be analyzed on two different days (HBC protocol). The dosing vehicle will be corn oil and hence analysis of the corn oil for peroxides will be conducted monthly.

Homogeneity

If more than one phase is present, duplicate analyses of homogeneity will be conducted at the high and low dosage group on samples taken from the top, middle and bottom of the mix. Homogeneity analyses will be repeated if the size of mix changes.

Stability

Stability of the test article in the dosing vehicle will be established on the low and high dosage groups at days 0, 7, 14, and 21 at two temperatures -- refrigerated and under conditions of use.

Concentration Analysis

Doses will be mixed at least weekly (or more often if indicated by stability data). Samples will be analyzed in duplicate prior to dosing on weeks 1, 5, 9 and 13 of the 90-day study.

Analyses will be repeated by the chemist if the duplicates are greater than 10% apart. If the results are greater than 10% from target the study director will be notified.

<u>Methodology</u>

It is proposed to analyze the samples for m-xylene by GC using a column containing Bentone 34. This has been used for many years to separate the xylenes. A new packing 5% SP-2100 1.75% Bentone 34 can apparently reduce the analysis time by 50% without any loss of resolution. We propose to use a Hewlett-Packard 5880A GC equipped with an autosampler, a microprocessor controlled data module and a flame ionization detector. We propose to use n-propyl benzene as an internal standard.

Reports

A brief interim progress report on chemistry will be issued prior to study start, followed by a more formal format as soon after the start as feasible. Concentration analyses will be reported on HLA/HBC Form 55 -- Analysis Report and Request Form. These reports will be incorporated into the final study report.

				n		
PRODUCT DESIGNATION	7					
	1					
Xylene						
Ayrene						
					•	
•					MA	TERI
SECTION 1. SOURCE & NOMENO	CLATURE		SA	FETY	ΠΔΤΔ	SHE
SPONSOR'S NAME			EMERGE	NCY TELEP	HONE NO	
ADDRESS (Number Street Con.	CA-1- 71 A		<u></u>			
ADDRESS (Number, Street, City,	State, Lip C	(ode)	,			
MOLECULAR WEIGHT			CHEMIC	AL CANATIN		
106.2			Aroma	AL FAMILY tic Hydrod	arbon	
CHEMICAL NAME AND SYNONYMS			FORMUL	A	, <u>a i D011</u>	
Xylol, Dimethyl benzene				`` C ₆ H ₄ (C	$H_3)_2$	
(Mixture of ortho, meta and pa SECTION 2. HAZARDOUS INGRE	ra isomers d	of Xylene)	· · · · · · · · · · · · · · · · ·			
SECTION 2. HAZARDOUS INGRE		LECTARI TOUSO				
BASIC MATERIAL	APPROXIMATE OR MAXIMUM	ESTABLISHED OSHA		LD ₅₀	Ļ	.D ₅₀
	Z WT. OR VOL.	STANDARD	ORAL	PERCUT.		
Xylene		100 ppm	Y		rat	4300 m
		= TIV				
		150 ppm	_			
		= STEL*				
* STEL = Short Term Exposure Lim	t -					
the max allowable conc not to	he exceede					
at any time during the 15 min.	excursion 1	imit				
	<u> </u>					
For m. Xylene:		<u> </u>				
SECTION 3. PHYSICAL DATA	Meta is the	major compone	ent of c	commercial	Xvlene	
BOILING POINT (°F)	i	VAPOR PRESSUI	RE (upma l	Hg.)		
MELTING POINT (PF)		10 mm @ 2	28.3°C			
-54° F		VAPOR DENSITY 3.66	(Aire	()		
SPECIFIC GRAVITY (H20=1)		EVAPORATION F	PATE /		:1)	
U.0/		CANLOIGHT TOUR	~15 (]		1)	
SOLUBILITY IN WATER (Pts/100 pts Insoluble	H ₂ 0)	VOLATILE		W W-1		
1113010016	6			% Vol.	<u> </u>	Wt.
APPEARANCE Clear liquid AND ODOR Similar to benzene and	toluene	SOLVENTS		_ •		
Social State of Benzene and	cordene j	Ur	ganic s	DIV.	·	
SECTION 4. FIRE & EXPLOSION	HAZARD D	ΣΑΤΑ				-
FLASH POINT CAR				FLAMMABLE	UPPE	R 7.0
1151100 0350	temperture	: 982 ⁰ F		(EXPLOSIVE	LOWE	
EXTINGUISHING Use Dry Chemical.	Water maybe	ineffective b				
SPECIAL FIRE FIGHTING Wear full-f	lace	merrective (pecause	of low fi	ash poi	nt
PROCEDURES vides eye protection.	are mask se	lf-contained b	preathir	ng apparat	us which	h pro-
UNUSUAL FIRE AND Material can	be ignited i	inder almost a	1 1000-	al tomos-	2 \$1100 5	
EXPLOSION HAZARDS Vapors formex	Diosive mixi	'urac in sim	A	£1 1 .		
	vel a consid	erable distan	ice to a	source o	<u>at. SDA)</u> f janit	on and
flash back.						

LBI-0082 4/77

MATERIAL SAFETY DATA SHEET

SECTION I

ำลูกเกิดcturer's Name)				-	
						· · · · · · · · · · · · · · · · · · ·
Chemical Name and Synonyms Xylene		Trade Name and Synon	yms			
(Xylol, Ethyl Benzene)			E	4 /		
Chemical Family Aromatic Hydrocarbonay be mixture of 0-, M-, and P-X	n V lene	<u></u>	Formula C ₆ H ₄ (CI	,3,5		
ay be mixture of 0-, 14-, and 1-x	y rene					
SECT	IÓN II	HAZAR	DOUS INGREDIENTS			
aints, Preservatives, & Solvents	%	TLV (Units)	Alloys and Metallic Coati	ngs	%	TLV (Units)
Pigments			Base Metal			
Catalyst			Alloys			
/ehicle			Metallic Coatings			
Solvents			Filler Metal plus	. –		
			Coating or Core Flux		+	
Additives			Others	<u> </u>		
Others 4"		>	<u> </u>			
Hazardous Mixtu	res of	Other Liq	uids, Solids and Gases		%	TLV (Units)
•						
						<u> </u>
	SECT	ION III PI	HYSICAL DATA			
Boiling Point (* F.)		291	Specific Gravity (H ₂ O = 1)			0.9
Vapor Pressure (mm Hg.) 8mm Hg @		72 ⁰	Percent Volatile By Volume (%)			
Vapor Density (Air = 1)		1.1	Evaporation Rate (= 1)			
Solubility in Water Insol.						
Appearance and Odor				•		
SECTION I	V FIR	E AND E	XPLOSION HAZARD DAT	' A		
		7		1 01	1 1	-1
Flash Point (Method Used) 81°-90°F	<u></u>	Flamm	nable Limits Lel Uel 1% 7		7%	
Extinguishing Media Dry chemical	, car	rbon dio	xide, foam			
Special Fire Fighting Procedures Avoid	cont	tact wit	h skin, wear self-con	tained bre	athin	g

PRODUCT DESIGNATION Xylene SECTION 5. HEALTH HAZARD DATA [IF AVAILABLE] TOXIC Inhalation - human TCL*: 200 ppm
TOXIC Inhalation - human TCL *: 200 ppm
TOXIC Inhalation - human TCL *: 200 ppm
OF ABSORPTION RELEVANT SYMPTOMS OF EXPOSURE headache, giddiness, vertigo, ataxia and tinnitus, confusion. EFFECTS OF Rabbits chronically exposed developed a decrease in the number of red blood CHRONIC EXPOSURE cells and leucocytes and an increase in the platelet count. EMERGENCY AND Remove from exposure. Wash affected body areas with copious amounts of soap and water. If eye is contaminated, flush with water for at leas 15 mins. Notify Medical Office immediately SECTION 6. REACTIVITY DATA CONDITIONS CONTRIBUTING TO INSTABILITY Normally stable CONDITIONS CONTRIBUTING None expected
RELEVANT SYMPTOMS Local irritation, CNS excitation and depression. Trasient euphoria, OF EXPOSURE headache, qiddiness, vertiqo, ataxia and tinnitus, confusion. EFFECTS OF Rabbits chronically exposed developed a decrease in the number of red blood CHRONIC EXPOSURE cells and leucocytes and an increase in the platelet count. EMERGENCY AND Remove from exposure. Wash affected body areas with copious amounts of soap and water. If eye is contaminated, flush with water for at leas 15 mins. Notify Medical Office immediately SECTION 6. REACTIVITY DATA CONDITIONS CONTRIBUTING TO INSTABILITY Normally stable CONDITIONS CONTRIBUTING None expected
CHRONIC EXPOSURE cells and leucocytes and an increase in the number of red blood EMERGENCY AND Remove from exposure. Wash affected body areas with copious amounts of soap and water. If eye is contaminated, flush with water for at leas 15 mins. Notify Medical Office immediately SECTION 6. REACTIVITY DATA CONDITIONS CONTRIBUTING TO INSTABILITY Normally stable CONDITIONS CONTRIBUTING TO HAZARDOUS POLYMERIZATION None expected
EMERGENCY AND Remove from exposure. Wash affected body areas with copious amounts of soap and water. If eye is contaminated, flush with water for at leas 15 mins. Notify Medical Office immediately SECTION 6. REACTIVITY DATA CONDITIONS CONTRIBUTING TO INSTABILITY Normally stable CONDITIONS CONTRIBUTING TO HAZARDOUS POLYMERIZATION None expected
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CONDITIONS CONTRIBUTING TO INSTABILITY Normally stable CONDITIONS CONTRIBUTING TO HAZARDOUS POLYMERIZATION None expected
CONDITIONS CONTRIBUTING TO HAZARDOUS POLYMERIZATION None expected
THEOREM
INCOMPATIBILETY (Materials to Avoid) Avoid oxidizing materials
HAZARDOUS DECOMPOSITION None expected
SECTION 7. SPILL OR LEAK PROCEDURES Eliminate all sources of ignition and flam STEPS TO BE TAKEN IN CASE MATERIAL IS RELEASED OR SPILLED WASTE DISPOSAL METHOD Incineration
SECTION 8. SPECIAL PROTECTION INFORMATION
VENTILATION REQUIREMENTS Transfer operations PROTECTIVE EQUIPMENT (Specify Types) LOCAL EXHAUST Should be done in chemical fume EYE Googles
MECHANICAL (General) Required hood. GLOVES Rubber gloves (neoprese) RESPIRATOR.
OTHER PROTECTIVE Lab coat RESPIRATOR Half-face respirator with cartr
SECTION 9. SPECIAL PRECAUTIONS
PRECAUTIONS TO BE Protect against physical damage. Outside or detached storage is TAKEN IN HANDLING preferrable. Inside storage should be in a standard flammable liquids storage room or cabinet.
OTHER PRECAUTIONS Separate from oxidizing materials.
Signature Oate Oate Address Office of Occupational Safety and Health

Office of Occupational
Lifty and Health

- 452 - SECTION V HEALTH HAZARD DATA

Threshold Limit Value . Effects of Overexposure	100 ppm Irritant to mucou	s membra	nes.	Gastroini	testinal disturbances, skin
Emergency and First Aid Call physician imme	d Procedures Remove f	rom expo	sure.	Administ	ter oxygen if respiratory distrand water. Discard wetted
clothing.	•				
	SECTION	N VI REA	CTIVI	Y DATA	
Stability	Unstable			Conditions	to Avoid
	Stable		х		·
Incompatibility (materia	is to avoid)Can_reac	t with o	xidiz	ors	·
Hazardous Decomposition	on Products			· · · · · · · · · · · · · · · · · · ·	
Hazardous May Occur			Cor	ditions to A	void
Polymerization 🚓	Will Not Occur	х			
Place into impervio Waste Disposal Method	ous container				bsorb on paper or bedding.
	SECTION VIII SPEC Specify type) <u>Half-ma</u> d conister at higher	sk resp	irator	with org	MATION anic vapor cartridges up
Ventilation	Local Exhaust Tr chemical fume hood		operat	ions in	Special
	Mechanical (General)			3 TO 11 TO 12 TO 1	Other
	ervious gloves			tection_ s or face	Avoid eye and face contact, we shield.
Other Protective Equipm	ent Protective cl	othing.			
	SECTION I	X SPECIA	AL PRE	CAUTIONS	
	n handling and storing				ted area. Away from heat,

PROTOCOL AMENDMENT



1330 -8 PICCARO ORIVI ACCKVILLE, MARYLAND 20

PROJECT NO. 2399-108 AMENDMENT NO.	DATE EFFECTIVE: May 20, 198
STUDY TITLE: Subchronic Toxicity Study i	in Rats with M-Xylene
	•
DISTRIBUTION ORIGINAL SIGNED PROTOCOL	TO BCO
DISTRIBUTION: ORIGINAL SIGNED PROTOCOL	
FIXED DISTRIBUTION: (No. Copies)* Health Services (1) Quality Assurance (1)	PERFORMING DEPARTMENTS (4 copies each Director
Compound Prep (Tox) (1) Contracts (1)	Toxicology (2) Analytical Chemistr
Scientific Res. (Tox) (20)x (1) Client Services (1) Lab Animal Medicine (1) Sponsor (1)	Pathology (5)
* Unless otherwise directed.	
Date and Means of Sponsor Authorization (if appropriate	v):
Amendment:	
, smortanene.	
Signed protocol forwarded by sponsor (s	signature page attached).
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	l
	Lay W. Wolfe
STUDY	DIRECTOR: Gary W. Wolfe, Ph.D.
	DATE:



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Project No. 2399-108

SIGNATURE PAGE

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Date: 3/14/86	

- 2/24/85